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FEAR*

PRESIDENTIAL ADDRESS

BUFORD G. HAMILTON, M.D., KANSAS CITY, MO.

LIFE would be a very drab existence were it not for our friends. It is the pleasures derived from association with friends, the unexpected kindnesses of friends, that silent understanding that exists between friends and doing for others that make life worth while.

This Society holds pleasant memories for me that will always be a sustaining stimulus for my own endeavors. I was present at the meeting in St. Louis when this Society was organized, and was made a member of the first executive committee. The first scientific meeting was held in Kansas City, for one day, in connection with the Kansas City Southwest Clinical Society. In the morning exclusive obstetric and gynecologic clinics were held in all the leading hospitals of greater Kansas City. In the afternoon, papers were given by distinguished members of this Society before some 1,000 general practitioners representing 22 states. This was pleasing to the founders of this Society since it was truly a missionary introduction for the Society in this area. This meeting was of special interest to the members of our specialty in Kansas City, since it was an opening wedge that separated obstetrics and gynecology from surgery in some of our hospitals.

At the meeting in New Orleans when you did me the very great honor to name me as your president for this year, I must confess I was deeply moved, since it is a great privilege to represent such a group as this one.

*Read at the Eighth Annual Meeting of the Central Association of Obstetricians and Gynecologists, Detroit, Mich., October 15 to 17, 1936.

NOTE: The Editor accepts no responsibility for the views and statements of authors as published in their "Original Communications."

Words fail me when I attempt to express my personal appreciation and also my appreciation of the Society's influence in behalf of our specialty in Kansas City. I only trust that you will believe me when I say I thank you.

Sentiment passes into insignificance when I recall that this Society was organized for a definite purpose and that from year to year it has carefully chosen its members to carry out this purpose. This Society is an offspring of illustrious parents—The American Gynecological Society and the American Association of Obstetricians, Gynecologists, and Abdominal Surgeons. These Societies have been very much interested in our activities and are interested in those members of this Society who might qualify to carry on the future activities and the traditions of the parent organizations.

At the christening of the Central Association, its future activities were dedicated mainly to the improvement of obstetrics in this section of the United States. Its sponsors were men whose horizon has been international, whose judgment sound, whose advice wise, and whose achievements class them as the noblemen of our specialty.

The previous leadership in this Society has been drawn from men well known in American obstetrics and men whose efforts have always been for the improvement of obstetrics.

The yearly meeting is an inherited custom of the parent organizations. The papers with their discussions represent the clinical and research progress made each year. These meetings have served still another important function, that of developing warm friendships. Such friendships serve not only to break down sectional barriers, but also serve to develop a oneness of thought and purpose. Such a leadership, with such a membership, so efficiently organized, should be eminently fitted to carry out the purpose for which the Society was organized; namely, the improvement of obstetrics in this special area.

A survey of the area with its problems brings out some interesting facts. Foremost are the criticisms made against American obstetrics. Our first impression is to be offended when criticisms are made and only tangible facts can change impressions. These facts are well borne out in the reports of the White House Conference and to a lesser degree in the reports from our own Society made in the last two years. Fortunately we have strong allies in the parent organizations and the American Committee on Maternal Welfare. It would seem that one of the first efforts of the individual member of this Society would be to see that his state has a strong maternal welfare committee, and that this committee would function with the State Society and the State Medical authorities in making each state committee efficient, to the end that all state committees would cooperate with Dr. Adair's committee for the improvement of obstetrics. From personal experience in the last two years in my home state, Missouri, I know it can be done and I would

emphasize the importance of cooperating with the State Medical Society and the State Medical authorities as a basis for efficiency. I can also assure you of the helpful assistance of Dr. Adair and his associate.

The members of this Society are known as specialists. Every state and county society and every hospital, indeed every woman in this area can be influenced and directed by the teachings and practice of this membership.

Critical as the statement may seem, I believe that we should accept the challenge that American and sectional maternal welfare problems belong to the specialist. As such we become the liaison between the medical school and the general profession in the improvement of obstetrics.

This becomes the more important when we review the activities of the American Board of Obstetrics and Gynecology. Each year this board, in qualifying those who may be called specialists, is making the requirements more stringent and is stressing the importance of the specialist's relation to the general practitioner. Therefore, it is of first importance that every member of this Society become a diplomate that he may have greater influence in his community.

Something of the magnitude of the undertaking of this Society may be appreciated when we recall that this area has a population of fifty-nine million people who represent our most typical American stock.

There are 16,089 doctors and 3,038 hospitals to care for this population. Then there are 37 medical schools that teach and train more physicians and specialists than any other similar area in the United States. Such a problem with such possibilities requires a beginning and an objective. Our beginning must be the individual physician or specialist and our objective the well woman and her well baby.

From a teaching viewpoint it is most difficult to analyze the teaching of students and their reactions to their training in private practice. It has been most fascinating to observe human behavior and obstetric behavior of both the physician and the specialist when accepting the responsibility for the care of expectant mothers. It would seem from the hours given for the teaching of obstetrics and the character of the teaching given that reason would obtain at all times. On the contrary there seems to be a particular emotion that supersedes reason where responsibilities are assumed. This emotion from its manifestations is recognized as fear. Many times when obstetric problems are discussed the statement is made that too often fear rather than reason directs procedure. For several years I have been an associate of students as an instructor, an associate of internes as a staff attendant, and an associate and consultant of the general profession. Often members of each of these groups when faced with obstetric responsibilities and defending a method or a procedure have justified their conduct by saying, "I was afraid." It may be said that this is only an inherited human weakness, since it is recorded that when father Adam was placed in the garden

of Eden he was surrounded with all that man could desire. However, the Master denied him one fruit, and as we know, he failed. Then it is recorded that when the Master asked him why he had not been equal to his one trust he replied, "I was afraid." All may not agree with this philosophy but rather with Williams who, when attempting to analyze human behavior said, "What reason should correct, all the training in the world will not improve a weak endowment."

As we attempt to define fear we may go far into the scientists' theories, most interesting yet confusing, especially so when we attempt to compare human behavior with obstetric behavior. A common conception of fear is that it is the response of an organism to a stimulus that may be injurious or destructive.

We are convinced from observing the prenatal, the natal, and the postnatal care of women that the problem is both moral and scientific. From this point of reasoning, we would suggest that fear is an inherited or acquired conception of right and wrong as is found in the philosophy of the teachings of the Master, that of doing unto others as you would have others do unto you.

From observing the attitude or the human behavior of physicians, we frequently assume that inheritance is the determining factor in their professional or obstetric reactions, yet as we observe the influence of environment, we finally conclude that both inheritance and environment are necessary for the development of the physician. Adair has suggested that the prenatal period should begin with the preconceptive period. From this philosophy we would suggest that doctors are born and not made, and that they are born of generations of integrity, of citizenship, and those accomplishments that contribute to the happiness and benefit of others.

Fear as applied to obstetric behavior might be said to be of two types: First, a trained, an intelligent, a reasoning, a courageous fear, and a fear for the right. Such fears have only one objective, the well woman and her well baby. Second, the untrained, the ignorant, the weak, the oscillating fear and the lack of fear for wrong—such fears are responsible for the invalidism of women and the loss of women and children. In its practical application it means that the trained, reasoning, courageous fear and the fear for right can only be influenced by errors of judgment. Such fears develop obstetric curiosity, investigation of problems or research, and an interest in everything that pertains to the improvement of obstetrics. The greatest enemy, the greatest obstruction, the greatest danger to maternal welfare is the weak, oscillating, thoughtless, ignorant, or wrong fears of both the trained and the untrained. If we are to search for the real offending organism that will grow, that can be plated into one definite group and proved by comparison, we would say that this wrong fear represents the offending organism in American obstetrics.

Take, if you will, the development of the physician and follow the possibilities of the two types of fears, especially those influenced or developed from environment. From infancy through primary school and high school, parental affections, discipline, and example develop courageous fears that direct behavior. From high school to the college or university is an epoch. A newly found freedom is encountered, an expression frequently made by students. In starting into medicine so many premedic hours are required and so many cultured hours are taken for an academic degree. Dr. Hutchins, president of the University of Chicago, has said that "The first two years of college work should be taken at junior colleges and at home, and if the student shows sufficient ability the last two years may then be taken in the university." This is a timely suggestion since home environment and home discipline are far superior to the influence of the so-called newly found freedom of the university. Then may I suggest that only the cultured hours be taken in the junior colleges, since many educators have suggested that few students know what profession to choose for their life work before their junior year. Also the parent may or will be cognizant of the situation and both time and money may be saved and disappointments avoided. The two years of home training and the added age will, without doubt, better fit the future doctor for premedical and medical training. Besides, as I will discuss later, we feel that the medical school should assume the responsibility for choosing those qualified to study medicine. The future doctor entering the university is the greatest idealist known, just clay, but how important the molding, since from the model is made a doctor or a specialist, of bronze, of marble, or of plaster. Again how important, since when placed in its permanent location, its beauty and its stability influence the professional, cultured, social, and spiritual life of that community.

Recently two nationally known medical educators were discussing this subject. The younger man's son was graduating from high school with high honors. The son had chosen a university described by his father as having an unusual social life. He spoke of the classes as being large and how impossible it would be for the professors to know the individual student. He also mentioned that the university was known for the friendships made on the campus and this influence on the financial future of its graduates. After this description of this university he asked this question, "If my son has the ability he seems to have, where would you send him for his university work, looking forward to his studying medicine?" The older man answered, "I sent my sons to a small university, where they had inspiring teachers and where the teachers knew my sons personally." It is of interest that his sons have both made superior records. He then made this very significant statement, "Your son's choice without doubt will be a great factor in his making money. His teachers, not being able to know him personally,

must judge his ability by his grades." The real boy cannot be measured by this method and I question the type of doctor developed from such an environment.

The premedical subjects are inspiring when presented by inspiring teachers. Unfortunately too often these subjects have become illegitimate subjects of illustrious parents and are presented by intellectual inebriates whose only marks of distinction are alphabetical notations. From many internes and recent graduates, we are told that certain ones of these emphasize the fact that their judgment of students determines the future doctors from that school. Unfortunately this attitude from an academic dialysis has escaped into the first two years of medicine. We find that for six years the would-be doctor is exposed to this environment and that he does not come in contact with doctors but for two years or at the most for two and a half years.

Another tragedy in developing doctors arises from the practice of certain schools accepting more students in the freshman year than can be cared for in the sophomore year. Their freshmen know that judgment is not passed on them by doctors but by the test tube, microscopic and academic would-be makers of doctors who judge too often from grades. May I ask what type of fears, what type of attitude toward human beings can be developed from such an environment? If hopes, honor, ambitions, and sentiments are stunted or paralyzed in attempting to make grades, only a sterile or materialistic attitude toward maternal welfare problems may be developed.

After graduation, internships become a most serious problem for both the school and the student. It would seem that when all schools require one year's internship before graduation and when hospitals are supervised by our national boards the problem will be solved. At the present time the private hospital internship in far too many instances is only an observation course. The lack of supervision and the lack of a common head develop false conceptions and habits that are important factors in our maternal welfare situation. We are having internes who before coming to our private hospitals have never been present at a home delivery. In a few instances we have had internes who have not so much as delivered one woman in the home or in the hospital. It is not infrequent in private hospitals without a clinical service that the interne will not deliver one woman while on the obstetric service. Somewhere in our course of training, students and internes must be required to follow patients through the entire course of labor, or the clinical course of labor cannot be known. It is my humble opinion that the one weak point in our training of students and internes is that not enough stress is placed on demonstrating the clinical course of labor, for it means staying at the bedside of patients during the entire course of labor. This is impossible in the unsupervised private hospitals

After graduation and internship, the state upon the completion of a satisfactory examination issues a certificate to practice medicine. The cost to the medical school for each graduate varies from \$800 to \$2,500 a year or \$3,200 to \$10,000 for the four years. The cost to the student varies from \$8,000 to \$15,000 for his academic and medical education, yet as we analyze his nine years of training, we find it is for only three or three and one-half years that doctors direct his training and that internships have little supervision other than those connected with teaching institutions. Yet they care for expectant mothers.

May I be pardoned for a suggestion that at present is Utopian in application? I intimated, from Dr. Hutchins' suggestion, that the first two years of college should be given in junior colleges and at home and that these hours be cultured hours. I would also suggest that the medical school authorities determine the fitness of students entering medicine by establishing a medical school campus where the future doctor will be taught or supervised by doctors and be associated with the teachers, staff members of the hospital, internes, medical students, and with all the organized agencies of medicine from the time he starts his pre-medical work.

Medicine is divided into two parts, the science of medicine and the art of medicine or people. In mentioning people I refer to their emotions and their problems. I refer to their emotions of love and hate, joy and sorrow, ambitions, hopes, and disappointments, to their problems whether they are physical, mental, economic, social, or spiritual.

To know these develops a love for people, a sympathy for people and a desire to do for people. Service becomes the major thought, and it is then and only then that the science and art of medicine can be practiced effectively. Otherwise service is only for the loaves and fishes. I am firmly of the belief that our materialistic attitude has caused us to lose sight of a class of people who have been the backbone of every man's success. I am also convinced that when people are thought of and cared for as suggested, state medicine will be forgotten and our clinical services will be in a great proportion supplanted with profitable patients. I do not hesitate to say that whatever success I may have attained to date, the greatest influence that I have had and the most lasting friendships that I have enjoyed have been among this forgotten class, the so-called poor.

So far we have only discussed the inherited and environmental development of the physician or specialist. May we turn for a time to his activities as factors that influence obstetric improvement?

We believe that labor with few exceptions is a normal physiologic process. We further believe that the only difference between physiologic and pathologic obstetrics in many instances is that greatest of all trained obstetric virtues, the ability to wait. We believe that it takes trained, intelligent, reasoning fears and a fear for right to appreciate physio-

logic reactions. Certainly we sympathize with the fears of the recent graduate and even with the recently trained specialist. It has always been of interest to me to note that the better training the physician has had the greater his fears have been.

The story is told of a distinguished obstetrician who was visiting a colleague in a neighboring city. At that time the colleague had a patient in labor with a posterior position. The membranes had ruptured prematurely, the cervix was hard and only partially dilated after twenty-four hours of pain with rest periods. However, the patient was in good condition. Later in the day the patient became tired, the pulse was 120, the head at the midstation, rotation was not completed, the cervix not completely dilated, and the host then asked his colleague to examine his patient and tell him what he thought best for the patient. This was done and the colleague advised to wait. The host, being tired and seeing how prolonged labor had been, said, "I have given the patient several rest periods. Do you think it is safe to wait?" Again the advice was for rest and to wait and still again if necessary. Later the patient delivered safely with the mother and child in good condition. The story appealed to me for three reasons. First: because these two nationally known teachers with large clinical experience were deeply concerned over a patient with a posterior position. Second: because the host appreciated the possibility of errors in judgment when tired and was amenable to advice and suggestion. Third: because they both had thorough training and experience, that rare virtue of decision to wait, and that trained courageous fear for the future health of the patient. Then it occurred to me that these are the attributes in physicians that determine their right to be classified as specialists and teachers of medical students.

It is agreed that the greatest number of women are being delivered in their homes and the question is being seriously asked, Can a woman be delivered as safely in the home as in the hospital? All would welcome the day when all women would be delivered in a hospital, but since the majority of women are delivered in the home, the question must be answered on its merits. From a rather large experience of ten years of home obstetrics, I must answer in the affirmative. Many times during these ten years mentioned I was called to see women in labor whom I had never seen before. If time permitted, I sent to my office or home for supplies; if it did not, it was possible to sterilize towels for draping the patient, prepare the patient, use rubber gloves and give an anesthetic. My own records show by comparison that women were equally as safe in the home as in the hospital. True, hospital conveniences and hospital privileges will be missed, yet it can be done. The only prophylactic measures that can be practiced are fundamentals; yet fundamentals are the same in the hospital, in the mansion, or in the hovel.

Our conception of right and wrong and our appreciation of service to people determine the safety of our application of fundamentals in the home or in the hospital.

It is also a fact that the majority of women in the United States are delivered by the general practitioner. Most often in discussing maternal welfare problems the general practitioner is given first place in our criticisms. This thought is worthy of serious consideration. That fundamental training in our schools has been the best, no one can deny. It is well to ask, Where did he interne? Who taught him that all these routines, selective operations and prophylactic procedures are fundamental and safe? Not our schools, but specialists, you and I taught him through the literature, through example, and through influence. Without question, this is a swamp that must be drained and reclaimed by the specialist.

I recall that in going from home obstetrics to hospital obstetrics I was influenced by specialists, older men, busy men and successful men and my patients were told by others in the hospital of all these prophylactic measures. Formerly in the home I had determined that patients could have their babies and upon my assurance, they expected that only time was necessary for delivery. My courageous fears gave way to competitive and economic fears and needless to say my results suffered until such a time as reason again supplanted fear. I mention these experiences since several of the younger men of this group have told me similar experiences. Our only measure of success must be by the yardstick of the well woman.

From almost every land where maternal welfare problems are being studied, the reports, with few exceptions, are that interference is our greatest factor in the loss of mothers and children. Yet there is a fundamental known to every nation where obstetrics is taught: that interference is to be done only in the interest of the mother or the baby. Quite old-fashioned, seemingly senile in its application, yet it is and always will be practical since it is right. Present-day trend seems to say this is a teaching for students but not for specialists. As has been intimated there have crept into our obstetric literature certain terms that are most alluring but dangerous, namely: Prophylactic measures, selective measures, routine measures, and measures for shortening or terminating labor. Probably at times all have been lulled to sleep by these time-saving measures only to find with the dawn of results not the well woman but the woman showing for days, months, or a lifetime the stigma of a procedure. It is now time to acknowledge that these procedures save the time only of the profession and that they should have a very limited place in the scientific and practical life of our obstetric family.

It must be granted that this group, because of their training, judgment and experience, can do all types of interference with skill and I

dare say most often with safety. Yet example, influence, writings, and discussion of these methods to or before other than this group or a similar group are directly harmful to the profession as a whole.

So much unwarranted space has recently been given to the subject of sedation that I hesitate to discuss it. Suffice to say that the success or failure of sedation rests with the scientific study and scientific application of the subject. We would urgently suggest that we as specialists do not put into print, discuss, or employ any means or method that has not first been proved to have, not only a scientific background, but a practical and safe application. The influence of the specialist is too far reaching to allow ourselves to influence or be influenced by any means or method that may be detrimental to any American mother.

It has been interesting to observe a hospital in my city that has been open to any member of the county Society. Ten thousand cases have been cared for by some 200 physicians. No physician has ever been denied the privilege of the hospital because of mistakes he may have made. From suggestion and assistance, mistakes have been remedied and individual obstetrics improved. It is most interesting that the statistics of this hospital have been a model for our other hospitals. I mention this hospital since the result has been attained through the efforts and influence of a member of this Society. I mention this record to show what a courageous fear for right, one person can create in any city, town, or community.

Some fifteen years ago a group in our city of which I was a member became interested in the induction of labor, or labor by appointment. Soon every medical society in western Missouri and eastern Kansas was deluged with papers. In time sufficient adverse data were gathered to restore reason, morbidity and mortality being the restorative agents. Thus, we have seen to our sorrow the dangers and folly of such teaching and practices. Even in the last year I have been quoted as advocating such a procedure. Surely "the evil that men do, lives after them."

I mention this experience to emphasize how lasting an influence papers, discussions, and demonstration may have on the profession as a whole and also to emphasize the fact that physicians with little or no training will attempt any method or procedure and justify their acts or procedure from papers or discussions of the specialist.

Another problem that mocks us and plagues us is the abortion situation. Dr. Litzenberg in his presidential address before the American Association of Obstetricians, Gynecologists and Abdominal Surgeons pointed out the dangers of our rapidly failing birth rate. From comparing our situation with the history of Rome and other great nations of the past he said, "We would soon face a national decay if our birth rate continued to fall as it is doing."

Dr. Fred Taussig has estimated that there are 700,000 abortions in the United States yearly with a loss of 10,000 women. Dr. Taussig does

not attempt to estimate the morbidity in these cases, the loss of blood, women with infections that get well, necessary and unnecessary operations and invalidism, that are so well known to each of us, and deaths that are indirectly caused from an abortion. Such a situation with such a mortality and such a morbidity is an obstetric plague. Such a record of smallpox, yellow fever, diphtheria, or typhoid fever would cause the state and national medical agencies to act at once. Contagious diseases have all been lessened in frequency or eliminated through efforts of the profession. Millions of dollars have been spent and many valuable lives sacrificed to eliminate disease that involves life. Yet it is a serious question as to whether or not the profession is directly or indirectly responsible for this obstetric plague.

We are faced with three problems:

First: Those accidental abortions that may be avoided by better prenatal care and a more intense study of the causes of accidental abortions. As we know, much progress is being made in this field.

Second: The therapeutic abortion! I refer to those done with the hope of conserving the lives and health of women. Dr. Adair quotes the child welfare bureau as stating that there is a 13 per cent mortality in therapeutic abortions. Such a statement causes us to ask seriously if it would not be better for the obstetricians to cooperate more with the specialists in the indicated lines of medicine in order that this 13 per cent mortality may be reduced to a minimum. With the exception of toxemias and nephritis most of the other serious indications have largely been superseded by improved medical treatment.

Third: The criminal abortion whether self- or medically produced and coming to us secondarily is a difficult and serious problem to the younger men and to many of the older members of our specialty. If the patient is a clinic patient it is well to care for her as seems best on our various clinical services. However, the cooperation of medical agencies with law agencies will reduce the excessive numbers we are caring for. In private practice there can be only one stand, that the patient go into a hospital and before witnesses write or sign a statement as to who did the abortion and how it was done. This relieves the reputable obstetrician and hospital of all criminal responsibility. The signed statement is then to be made a part of the hospital record. The speaker has followed this routine for several years with perfect satisfaction to himself and I also know that this plan is followed successfully by many others of our specialty. I would further advocate that all abortions from whatever cause should have a separate certificate or report that must be a part of our health agencies' record.

The destruction of 700,000 defenseless lives yearly and 10,000 known mothers is an obstetric plague, more revolting in its aspect than any

plague or epidemic yet known. The more so since it not only involves the populating of our nation but the decay of our nation, mentally, physically, and spiritually.

Too much encouragement cannot be given to the intensive study and investigation of accidental abortions in view of the efficient results already reported. A 13 per cent mortality in therapeutic abortions as reported from the Children's Bureau is scientifically too high. I am of the belief that too much emphasis is given to the subject in the literature, not so much by those whose fears for the right are so well known, but by those whose fears of wrong seem to be lost in the quest for gold. Unfortunately these use their interpretation of the literature as a smoke screen to hide their death-dealing practice, and this screen may hide causes involved in the 13 per cent mortality of so-called therapeutic abortions.

Such a plague requires strict quarantine. No better prophylactic or preventive measure could be instituted than the cooperation of medical agencies with law-enforcing agencies.

Two types of infected areas are found. First, those of the profession without organized medicine. As we have observed, these are the Anopheles type that are filling up our clinical services. Only the oil of law-enforcing agencies can destroy their breeding places. The second group belong to organized medicine. These should receive the same treatment offered through law-enforcing agencies. Besides this, a preventive measure would be professional ostracism. The popularity of these is due to their professional standing and the safety for social inconveniences found in the hospitals that admit this group without questioning their procedures. This group preys on the intelligentsia group and teach them their modern term of social inconveniences. This group of people are of importance since they so thoroughly represent the truly American stock and are the ones who should have children. Aside from mental and physical qualification they are amply able to provide for children. As we observe the decreasing number of children in such families, we cannot refrain from asking, Is childbearing and the responsibility of caring for children quite as much a sociologic factor in the happiness of the home as those problems associated with idleness in the home?

Like all plagues and epidemics the success of quarantine and prevention depends upon the cooperation of the individual physician and specialist. The treatment to be applied by the individual physician or specialist is best expressed by a colleague of mine, Dr. Calkins, who said, "Cool and considerate reasoning must supplant social and economic dictation and weak-kneed accession to the importation of influential patients."

In the discussion of obstetric fears, I trust I may be pardoned for sentimental flights. However, this Society's chief purpose in organiza-

tion was for the improvement of obstetrics in this area. Our beginning was the individual physician or specialist and our objective the life and health of the mothers and their offsprings. We have advocated that this is a moral problem as well as a scientific problem. Therefore, sentiment cannot be eliminated as the ruling emotion in its solution. No one can question the motives of the sponsors of this Society, representing as they have the parent organizations, the American Gynecological Society and the American Association of Obstetricians, Gynecologists and Abdominal Surgeons. No one can question the efficiency of this organization nor its previous leadership. The function of the Society and the manner in which it solves its problems will, however, determine its success.

Each state in this area may have a well-organized and well-functioning maternal welfare committee. Every member of this Society may be certified by our American Board as a specialist in our specialty, yet in the last analysis the problem becomes the relation of the individual physician or specialist to the individual expectant mother.

In my humble opinion a trained, an intelligent, a reasoning, a courageous fear, and a fear of right must be the qualifications of the individual physician or specialist caring for women during the prenatal, natal, and postnatal periods.

Is it asking too much, is it stating the situation too emphatically, to say the problem is ours as specialists? That as specialists we are the liaison between the school and the general profession? Is our philosophy entirely wrong when we say that obstetric fears are largely responsible for our standing among the nations in maternal morbidity and mortality? Again is our philosophy of obstetric fears entirely wrong when we advocate that obstetric fear is an inherited or acquired conception of right and wrong based on the teaching of the Great Physician?

1107 BRYANT BUILDING

Buchner, E. F., Jr.: The Rate of Growth Before Birth, J. Tenn. M. A. 29: 131, 1936.

Plotting the averages of all available curves of anatomic and radiographic measurements on the same coordinates, together with the curve of the probability of survival, as derived for want of authoritative figures from the generally accepted clinical impression, resulted in a graph of considerable practical value in obstetrics and pediatrics. Allowing for errors in draftsmanship both the length and weight do not increase as smooth curves, and anatomic and radiographic measurements of the head parallel each other fairly closely.

It is suggested that this graph, together with immediate length and weight measurements of the newborn child, may help in the quick and more accurate determination of the stage of its development.

J. P. GREENHILL.

THE SURGICAL TREATMENT OF COMPLETE PERINEAL TEARS IN THE FEMALE*

NORMAN F. MILLER, M.D., AND WILLIS BROWN, M.D., ANN ARBOR, MICH.
(From the Department of Obstetrics and Gynecology, University of Michigan)

RELUCTANTLY indeed does the cold gray past reveal its secrets. From its silent depths come only patchy fragments, telltale evidences, from which we may construct our concept of remote gynecology. Since earliest times, tearing of the rectum at the time of parturition has been looked upon as a most depressing accident—saddening to the patient, despairing to the physician, and always necessitating a gloomy prognosis. Cure depended on the generosity of nature, on binding the legs together and on such other traditional remedies as existed at the time. Indeed this appears to have been the prevailing method of treatment for centuries, and it continued long after surgical union had first been tried.

As late as 1840 Payan recommended confinement to bed for six weeks, the patient to be kept on her side and her legs tied together. In 1864 Robinson advocated similar treatment, but was less emphatic as to its efficacy, merely suggesting that it be tried before operation was undertaken. These probably represent late and more or less isolated uses of posture treatment. Guillemeau, a student and contemporary of Ambroise Paré (1510-1590), was probably the first to attempt surgical union of a completely ruptured perineum. Later, Mauriceau (1637-1709) and Smellie (1697-1763) recommended operation and suturing, but there is no evidence to show that they ever performed restoration by this method. General acceptance of suturing was inevitable but slow. Saucerotte's notable contribution appeared in 1798, and Mentzel described a button suture for this purpose during the same year, Figs. 1 to 7. In 1801 Nedel told of freshening and approximating the edges. He also recommended fat and oil applications with soft massaging to make the perineum more yielding and less likely to tear. That operation was still something of a last resort is suggested by Wendelstadt's description of a case which he treated in 1803. The wound was cleansed and the legs were tied together, but due to exhaustion from sleeplessness and constant irritation from diarrhea, the legs had to be loosened and this form of treatment given up. Later the edges of the wound were pared and approximated with strong wax thread.

Notwithstanding the fact that surgical correction was known it was not until half a century later that reports of surgical cures commenced to occupy a conspicuous place in medical literature. Among the many prominent names of this era we find Jobert, Tragher, Maisonneuve, Verhaeghe, Tanner, and Laugier. With surgical treatment so generally accepted we pick up new threads emanating from scientific discoveries

*Read at the Eighth Annual Meeting of the Central Association of Obstetricians and Gynecologists, Detroit, Mich., October 15 to 17, 1936.

of the times. The use of chloroform is mentioned and more attention is given to anatomic restoration of the perineal body and to special technical improvements. Since the need for avoiding tension was recognized even before the application of suturing, it is hardly to be expected that this fundamental principle should be discarded with the acceptance of surgical restoration. Tying the legs together was still used in conjunction with suturing. As refinements in technique continued, we find many incidental controversies arising. The matter of diet and postoperative care of the bowel became a matter of con-

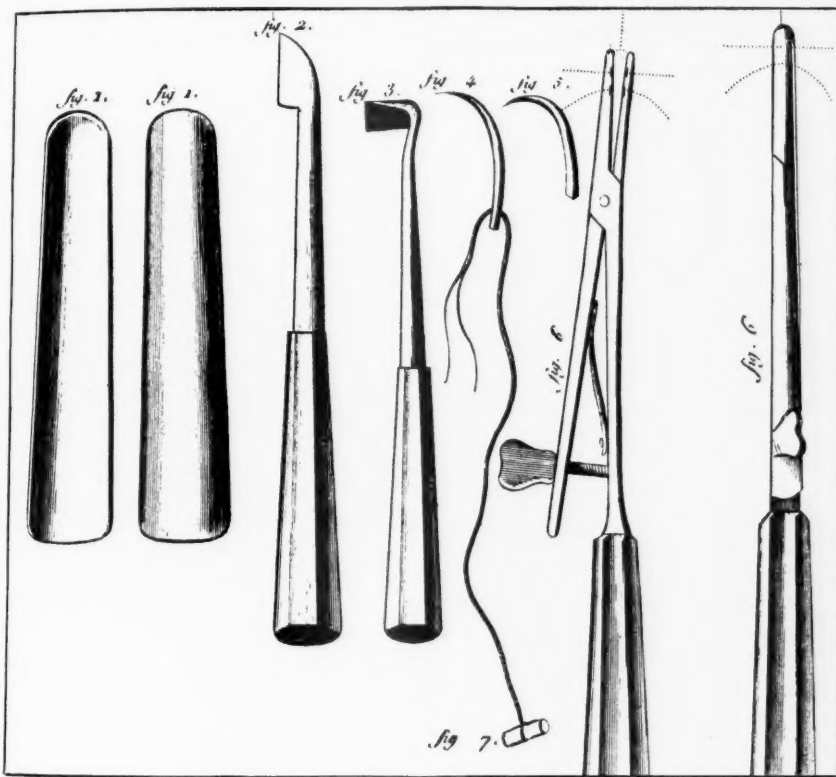


Fig. 1.—Instruments devised by Saucerotte for use in the repair of complete tears of the perineum (1798).

tention; there was about an even division for and against the use of opium following operation. Now, too, we see the ancient quill losing favor, Hicks and Bryant in 1862 being among the first to discard it for the ordinary suture. It is with regret indeed that we must pass rapidly through this notable era, the historian's paradise.

Most noteworthy, perhaps, among the contributions of the last half of the nineteenth century were those of I. Baker Brown and our distinguished D. H. Agnew (1868) and J. C. Warren (1882) whose meritorious contributions will long be treasured.

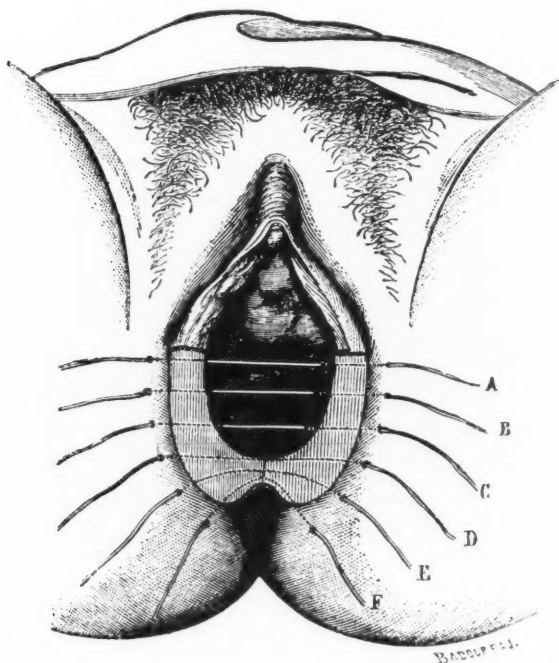


Fig. 2.—Technique of perineal repair about 1870. (From Arch. de Tocologie, 1876.)

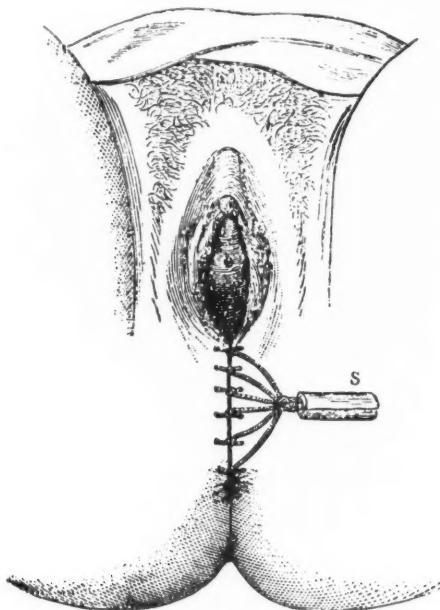


Fig. 3.—Technique of perineal repair about 1870. (From Arch. de Tocologie, 1876.)

Ristine, Noble and Kelly inaugurated twentieth century practice with modifications of the flap operation, a procedure which today continues to be among the most satisfactory methods for repair. By then, however, the pendulum had reached the center of its arc, for interest in this subject seemed to fall off. An occasional revival of the subject is found in the reports of Hall, III, Hamner, Goldspoon, Phaneuf, Smith and Linton, and Royston.

Our own study is based on 182 chronic complete tears treated at the University of Michigan Hospital. No acute tears are included. The cases studied are divided into two groups, i.e., those operated upon by various methods prior to 1931, comprising 144 cases (Group I); and 38 patients operated upon since 1931 by what we speak of as

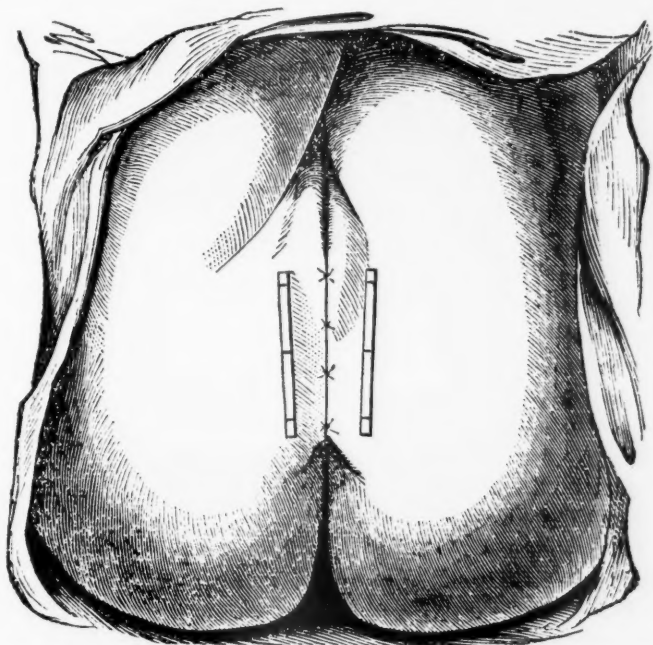


Fig. 4.—Perineal closure advocated by J. T. Bradford. (Cincin. Lancet and Obst., 1869.)

the *paradoxical operation* (Group II). The operative techniques used in the cases of Group I are difficult to name because of their general similarity but included those in vogue during the early years of the twentieth century (1901-1931). At first what was known as the Emmett operation was preferred; that gradually gave way to the flap technique described by Warren (1882), Ristine (1900), and in 1902, by Noble. Minor variations were common but basically the above procedures were used for the thirty-year period, providing the Group I cases. Since July 1, 1931, all third-degree tears (Group II) which we have treated have been repaired by what is fundamentally the flap

operation combined with subcutaneous cutting of the sphincter. This latter step explains our term *paradoxical operation*. Preoperative preparation and postoperative care generally applied to Group II cases (those repaired by paradoxical method) may be outlined as follows:

Preoperative: (1) One ounce of castor oil daily for three days prior to operation. (2) Soapsuds enema on day prior to and morning of operation. Repeated until return is clear. (3) Low residue diet commencing three days before operation, and clear liquids only on day before operation.

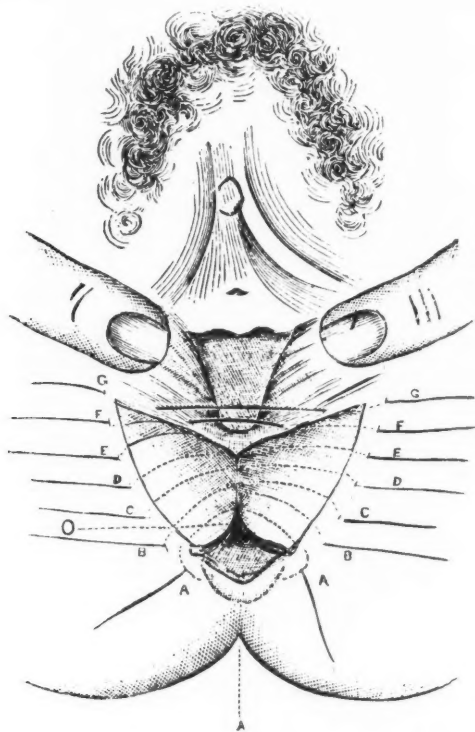


Fig. 5.—Repair of complete laceration. (H. T. Hanks, The Medical Record, 1882.)

Postoperative: (1) Clear liquids for nine days. (2) Any liquids on tenth day and soft diet on the eleventh. (3) One teaspoonful of paregoric four times daily for first nine days. (4) Retention oil enema daily commencing tenth day after operation. (5) One ounce of castor oil by mouth on twelfth day.

Our preoperative preparation of patients with third-degree tears may appear unnecessarily elaborate. It represents an effort to minimize the danger of infection and to make the patient comfortable. By thorough evacuation of the bowel, there is less likelihood of contamination, and peristalsis during convalescence is reduced. The need for tying up the bowel postoperatively is not unanimously agreed to in the literature and may well deserve further study.

The steps of the paradoxical operation are shown in Figs. 8 to 14. Locating the sphincter ends, particularly in old cases, is facilitated by digital palpation of the sphincter through the anus when exploring with a blunt curved hemostat as shown in Fig. 14.

Since tension is to be released by cutting the sphincter, only two No. 1 chromic stitches are used for approximating the muscle ends. Cutting the sphincter directly posterior does not appear to relieve tension sufficiently because of the close intermingling and attachment of the posterior levator ani muscle fibers converging toward their coccygeal

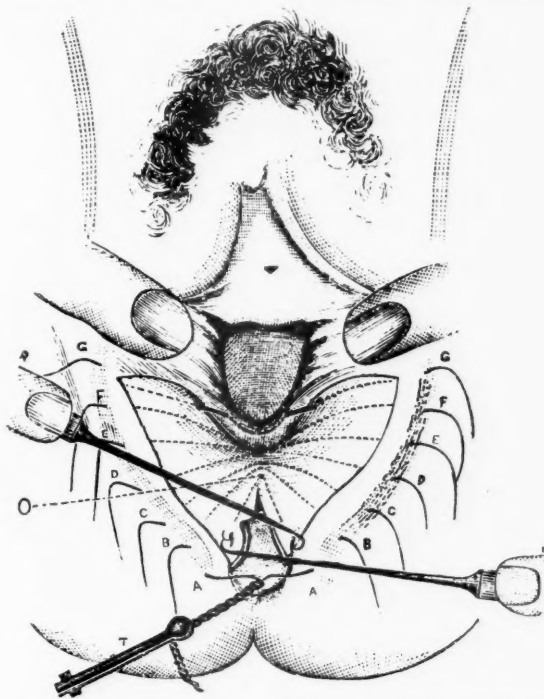


Fig. 6.—Repair of complete laceration. (H. T. Hanks, *The Medical Record*, 1882.)

attachment. In long standing cases, the sphincter may be cut as the initial step, thereby facilitating approximation of the anterior sphincter ends.

At least three fundamental principles are essential to successful plastic surgery; namely, (1) good blood supply, (2) absence of infection, and (3) avoidance of tension. The first fundamental, good blood supply, scarcely need be commented upon. Probably no one technique or procedure is very much better than another in this respect, yet adequate blood supply is extremely important and is fortunately present in the perineum, except in badly scarred, often-operated cases. Excessive cicatrix may often be excised or incised if necessary

as a preliminary operation. Of real significance in this connection is the fact that each unsuccessful attempt at repair leads to more scarring and lessens the chances for success in later attempts, a fact to be borne in mind by every physician who contemplates the repair of a third-degree tear.

Since the operative site in every complete tear is always potentially infected, painstaking precautions to avoid excessive contamination are always wise. It is here, perhaps, that the flap technique is of greatest value. Not only does the flap adequately provide for the

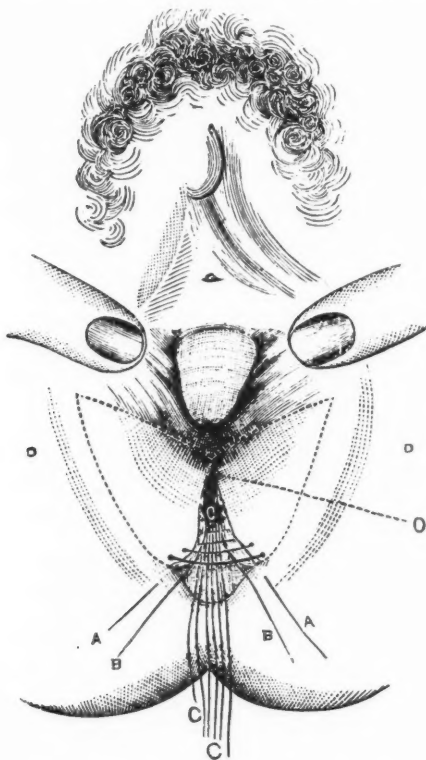


Fig. 7.—Repair of complete laceration. (*H. T. Hanks, The Medical Record, 1882.*)

deficit in the anterior rectal wall in most cases but in addition it forms an intact protective barrier against contamination of the operative field. Any redundant or excessive mucous membrane may be excised during the final steps of the operation. It is because it more nearly fulfills the second demand of sound plastic surgery that we prefer the flap technique.

The importance of relieving tension was apparently well recognized by the earliest operators. Noteworthy early attempts to minimize tension are seen in the tying together of the legs and in Dieffen-

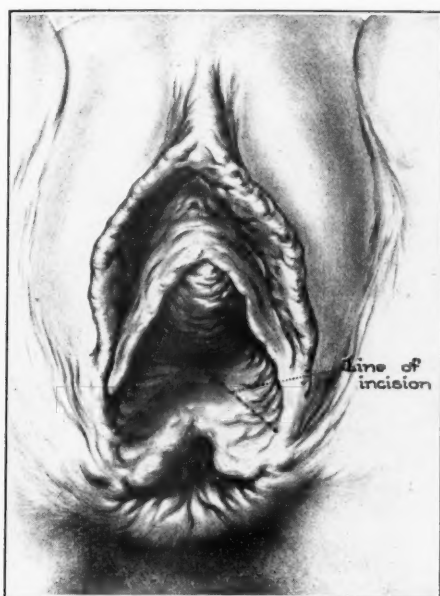


Fig. 8.—Showing line of incision for developing flap.

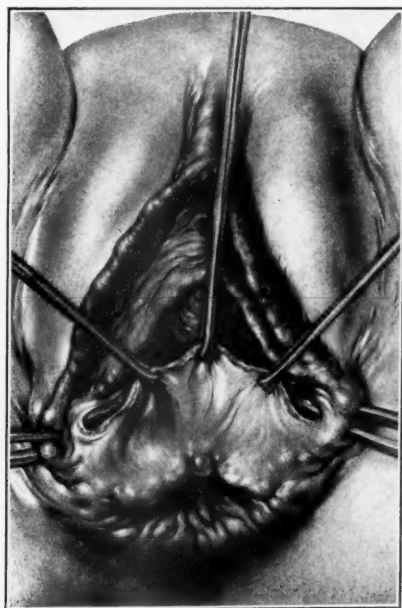


Fig. 9.—Dissection of flap completed.

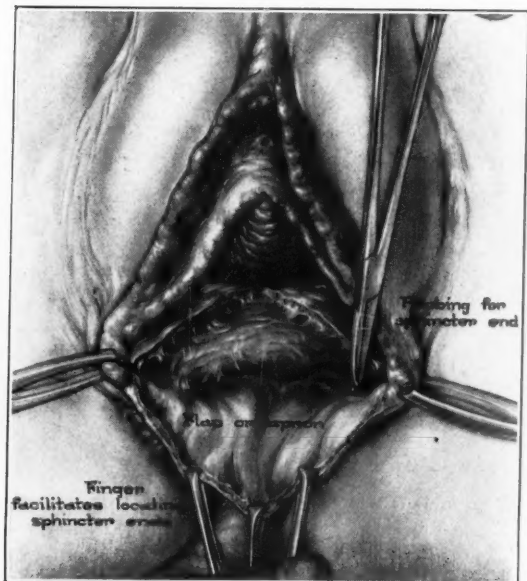


Fig. 10.—Probing for the sphincter end. Note how flap or apron tends to protect operative field. In the majority of cases the flap also adequately provides for the deficit in the anterior rectal wall.

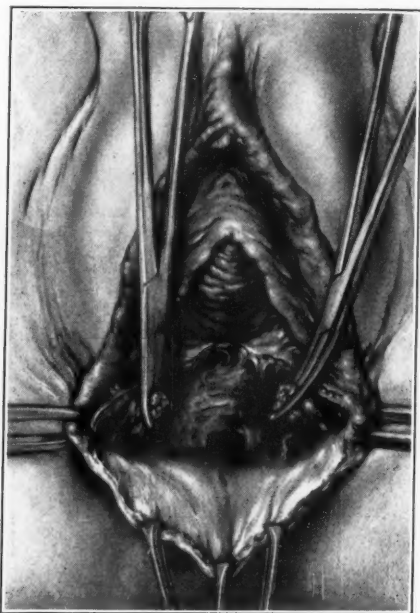


Fig. 11.—In about one-half of the cases the sphincter ends are readily isolated. In others it is necessary to take adjacent levator fibers.



Fig. 12.—Approximation of the sphincter ends may be facilitated by early cutting of the sphincter.

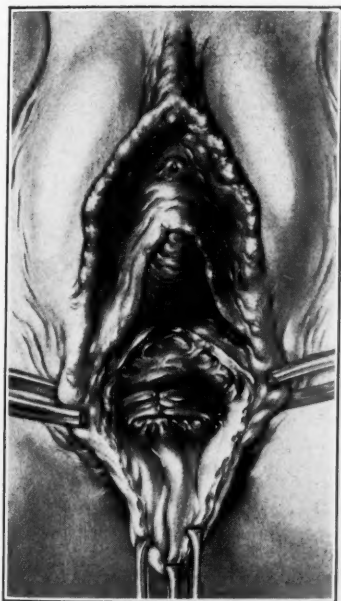


Fig. 13.

Fig. 13.—Since there remains little tension on the anteriorly united sphincter, only two chromic No. 1 sutures are used to keep the ends in apposition.

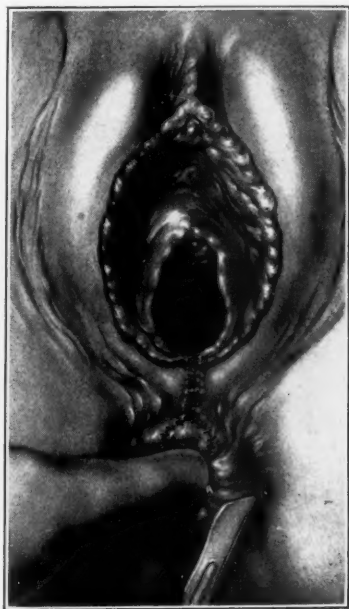


Fig. 14.

Fig. 14.—In the average case the operation is completed by subcutaneous cutting of the sphincter in the posterior quadrant.

bach's incisions. When first we cut the sphincter for release of tension, we thought it might be original but extensive study of the literature revealed that this was a very old and well-proved procedure.

Imagine, if you can, an operating setup half a century before the world knew of Pasteur and infection, seventy-five years before the illustrious Lister and antisepsis, decades before the discovery of chloroform. Take away the surgical knowledge acquired in the past 150 years, and we have the situation faced by the stern but courageous Saucerotte and his able assistants, Castara and Rousel. It was no mean problem that caused them concern that day in the year 1798. Their patient, now forty days postpartum, demanded something be done for the unbearable fecal incontinence. Posture and other traditional remedies had proved valueless. A first fruitless attempt with the then almost unheard-of suture method had failed. Impelled by the undaunted spirit of their patient, these courageous pioneers again undertook repair, but this time at the suggestion of one of the assistants the sphincter was cut in order to release tension. There followed days of anxious waiting, needless as it proved, for their patient was cured. But Saucerotte and his assistants were far ahead of their time and the real value of their contribution did not become known until popularized by such illustrious men as I. Baker Brown, Chassaignac, Hugnier, Mercier, and Velpeau. The principle of release of tension was generally recognized but severing the sphincter was by no means the only accepted method. Some preferred the semilunar incisions of Jobert and Dieffenbach, others the tension suture. While Brown's astonishing results in 75 cases reported in 1860 must be looked upon as the work of a remarkably skillful operator, Brown himself attributed much of his success to his practice of cutting the sphincter.

Comparison of results obtained by various operative techniques is complicated by the fact that there appears to be no generally accepted criteria or standard of cure. As the terms used in describing the results are often relative, it is difficult to know just how good a "satisfactory result" really may be. There is need for a better grading of results, and for general acceptance of such grading. Another factor in determining the value of any one method is the end or late result of operation. One does not always achieve nor should one expect immediate and perfect functioning from a sphincter which has remained functionless for many years. Consequently, follow-up examinations might well show a higher degree of success than reports based on immediate postoperative evidence.

We are opposed to the use of such terms as "cured," "excellent," or "good," because these terms permit wide range of interpretation. In this study the term *function restored* is applied to all cases where control over the fecal stream is regained. In some cases of this group

the control over gas was not entirely satisfactory, but sphincteric action was restored. So-called *perfect* results are common following repair of fresh complete tears, but in old and long-standing cases, we believe that examination two weeks postoperative does not always show sufficient return of sphincter activity to permit of complete control of gas. By *function improved* we mean control over solid or normal stools but imperfect or no control of gas or liquid stools. *Failure* of course means no control whatsoever, even though the perineum may appear well reconstructed. The *unknown* results applied to 5 per cent of Group I cases occurred early in the series and no results were recorded in the history. These may have been failures but for lack of evidence it appears wiser to classify the result as unknown. We believe the terms used to designate result and the criteria upon which they are based are reasonable, and we suggest their use in future reports.

Questionnaire follow-up was attempted in this series but was unsatisfactory. The number of replies from early cases were too few to be of value. Our data then are based on results noted at the time of discharge from the hospital. If improvement does occur weeks after operation in old chronic cases, then we may reasonably assume a higher incidence of cures, especially in those treated by the paradoxical operation. Many of our patients had suffered fecal incontinence for fifteen years or more, the longest being thirty-three years. The average duration of the tear was nine years.

TABLE I. GENERAL DATA

Average age of patients	33 years
Average duration of tear	9 years
Average parity	3.4 per cent

TABLE II. ETIOLOGY

	NUMBER	PER CENT
Nonoperative delivery	46	25.00
Operative delivery	126	69.00
Surgery	7	4.00
Etiology unknown	3	2.00
	182	100.00

In discussing results one cannot overlook the fact that previous unsuccessful operation with incidental scarring increases the technical difficulties and reduces the prognosis for return of function. Note that 40 per cent of Group I, and 63 per cent of Group II cases had undergone operation one to six times prior to admittance to the University Hospital (Table III).

Furthermore, we believe that in any evaluation of results due credit must be given the levator ani muscles which are utilized in building up

TABLE III. NUMBER OF OPERATIONS PRIOR TO ADMITTANCE

NO. OF OPERATIONS	GROUP I*	GROUP II†
I	55	18
II	8	4
III	2	1
IV	0	0
V	2	0
VI	0	1

*The 67 patients in Group I operated upon once or more prior to admittance averaged 1.3 operations per patient.

†Twenty-four of the 38 patients finally treated by paradoxical methods averaged 1.5 operations per patient prior to admittance.

the perineum. Complete cure and perfect control occur as the result of an intact sphincter but many patients seem to do remarkably well once their levators become properly trained and adequately developed.

Results obtained in our series of 182 cases are shown in Table IV.

TABLE IV. RESULTS

	GROUP I	GROUP II
Function restored	71.00%	87.00%
Function improved	15.00	8.00
Failure	10.00	5.00
Unknown	5.00	0.00

We attribute the higher incidence of cures in Group II (paradoxical repairs) to the release of tension on the anteriorly united sphincter.

Unfortunately a general comparison of results is not possible. There is a noticeable lack of recorded results in the literature and, as previously stated, those which do appear fail to make a decisive grading. Definite commitment concerning results obtained is essential if we are to make healthy comparisons with the hope of ultimately being able to arrive at the most desirable method of repair.

SUMMARY

1. Historic highlights in the treatment of third-degree tears are revealed.
2. Surgical principles pertinent to the correction of third-degree lacerations are discussed.
3. Data on the results of treatment in 182 patients are presented.
4. The need for a universal standard in appraising results of treatment is pointed out and certain criteria and terminology are suggested.
5. The *paradoxical repair* (flap operation plus sphincter cutting) is illustrated.
6. It is hoped that results following other methods of operative correction will be reported in order that we may ultimately determine the most satisfactory method of repair.
7. An extensive bibliography is appended.

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Yeast-like organisms isolated from vulvovaginitis and oral thrush were run through the fermentation tests and allowed to grow on Sabouraud's dextrose agar plates for observation of morphology. Those organisms failing to produce mycelium were called cryptococcus and those producing mycelium, monilia.

Classifications of these organisms were made by correlation of fermentation and morphology. Fermentation groups were determined in 8 cryptococcus and 73 monilia strains isolated from vulvovaginitis of adults and oral thrush of infants.

W. B. SERBIN.

SIX NORMAL AND COMPLETE PRESOMITE HUMAN OVA*

JOHN I. BREWER, M.D., PH.D., AND JAMES E. FITZGERALD, M.D.,
CHICAGO, ILL.

(From the Department of Obstetrics and Gynecology and the Henry Baird Favill Laboratory of St. Luke's Hospital, and the Department of Obstetrics and Gynecology of Northwestern University Medical School)

THE possession of six perfectly preserved, stained, and serially sectioned presumite human ova of different ages in one laboratory affords excellent material for detailed study of implantation, early placentation, and embryonic development. There are approximately 75 presumite human ova reported in the world literature. The majority, however, are of little value. Only 30 have sufficient data and are normal enough to permit the drawing of conclusions. Only a few are anatomically complete and sectioned favorably. Interpretation of the findings have been reported by such a diversified group of workers that uniformity is lacking. To obviate this, Grosser, Streeter, Teacher, Bryce, Florian and Hill, and others have made collective studies of all the presumite ova to which they have had access.

Our group comprises six presumite ova, all of which were obtained by hysterectomy. In none was there any abnormality of the pregnancy. This is important in considering the actual stage of development. All were fixed within ten minutes after clamping the uterine blood supply. Each was sectioned and arranged serially. Four were oriented so that the embryonic disc was cut in cross-section and two were cut sagittally. There were no sections lost in any of the specimens. Various fixing solutions and stains were used. One ovum, the Jones-Brewer I, is the youngest human ovum to have cytologic methods applied to placentation. The Edwards-Jones-Brewer specimen is the youngest normal and anatomically complete ovum to be reported in the United States.

The latter is particularly adapted to a study of implantation because all sections include the entire thickness of the endometrium and a portion of myometrium. This makes possible a complete study of the vascular phenomena. Trophoblastic activity is equally well investigated in this ovum and the next youngest of our group, the Jones-Brewer I ovum.

VASCULAR PHENOMENA

The vascular changes in the endometrium of early pregnancies are identical to those phenomena in the normal menstrual cycle (Brewer).

*The Prize Award paper, read at the Eighth Annual Meeting of the Central Association of Obstetricians and Gynecologists, Detroit, Mich., October 15 to 17, 1936. Aided by a grant from Mrs. Emmons Blaine and from the Rockefeller Institute to the University of Chicago.

The changes in the endometrium in various phases of the normal cycle have been described recently by Bartelmez, Markee, Daron, and others. As Bartelmez points out, the essential characteristics of menstruation are extravasation of blood and necrosis of the superficial zone. Lahm in 1926 had already demonstrated constriction in the long spiral arteries with a resultant superficial necrosis of the endometrium. Meyer-Rügge and Markee substantiated these findings. Markee's work, based on observation in endometrial transplants in the anterior chamber of the eye in monkeys, conclusively proved the occurrence of vasoconstriction. The blanching phase dependent on vasoconstriction was increased markedly as the time of menstruation approached. The vasoconstriction with consequent ischemia lasting twelve hours or longer, he states, is sufficient to produce extravasation of blood and necrosis. The extravasation is usually quite superficial. Substantial evidence of vasoconstriction during the bleeding phase of menstruation was presented by Bartelmez. In his specimens he observed and pictured spiral arteries with open lumina projecting into the uterine cavity without hemorrhage about them and without blood in their lumina. These facts explain the means by which the bleeding at menstruation is controlled. It has been shown by Daron that the basal portion of the endometrium and the more peripheral portion are supplied by two distinctly separate types of arteries. His conclusions were based upon the fact that the arteries supplying the basal portion of the endometrium were less coiled and did not present the phenomena of vasoconstriction. The spiral arteries extending to the surface of the endometrium, he found, did undergo vasoconstriction.

The vascular changes in the endometrium during its cycle are not for the purpose of producing changes incident to menstruation, but rather are a preparation of a site for the implantation of the human ovum. This was suggested by Brewer in his observation on the Edwards-Jones-Brewer ovum. He showed that vasoconstriction of the long spiral arteries was frequent in the region of the implanted ovum. (Fig. 1.) The superficial portion of the arterial and venous systems was frequently congested in association with vasoconstriction of the basal portions. The extravasation of blood is found only superficially (Fig. 2).

The large amount of blood in the Edwards-Jones-Brewer ovum could be accounted for if one assumes that the patient was operated upon during or immediately following a period of blush (Fig. 2). Vasoconstriction produces superficial necrosis of maternal tissue in the region of the implanted ovum similar to that noted in the pseudopregnant endometrium. This is proved by the observation of necrosis of maternal tissues some distance from fetal trophoblast.

Throughout most of the superficial portion of the pseudopregnant endometrium, vasoconstriction, formation and congestion of super-

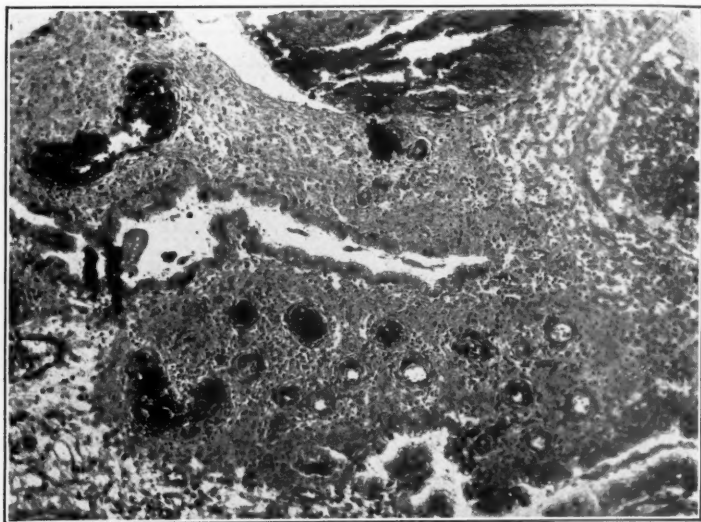


Fig. 1.—The Edwards-Jones-Brewer ovum. This photomicrograph demonstrates the phenomenon of vasoconstriction. The spiral artery near the penetration zone has divided into two branches that extend parallel to one another. They are seen near their origin. One is dilated and filled with blood while the other is constricted near its origin and is empty. Such findings are frequent.

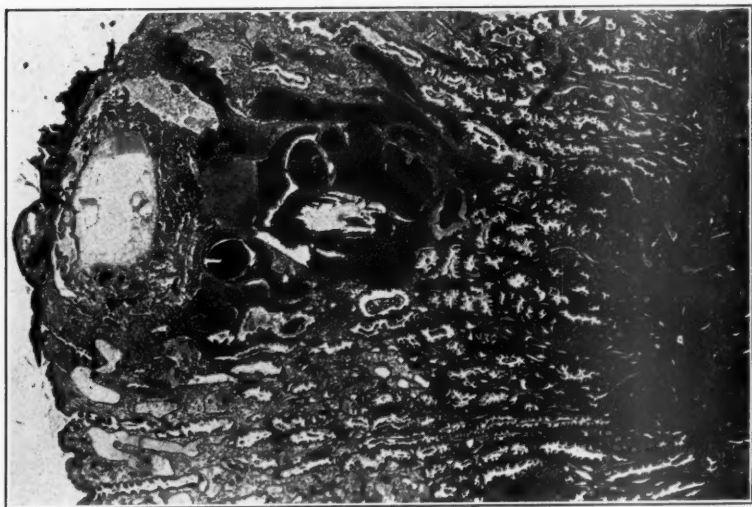


Fig. 2.—The Edwards-Jones-Brewer ovum. The photomicrograph shows the blastocyst embedded superficially in the decidua. The embryonic anlage is located at the most dependent pole. The surface coagulum is torn in part. About the blastocyst there are numerous dilated venous sinuses. There is a large basal sinus filled with blood which is connected to the large lateral sinuses. The basal glands are in many instances filled with blood.

The endometrial glands are the typical glands of pregnancy. Spiral arteries are traced to the endometrial surface except in the region of the blastocyst.

The myometrium contains a large spiral artery near its origin. It is located directly beneath the implantation site and accounts in part for the extensive hemorrhage noted in this specimen.

ficial venous sinuses, superficial extravasation of blood, hemorrhage and superficial necrosis are consistently found, whereas, in early implantation (Edwards-Jones-Brewer ovum) these phenomena are limited to the region of the implantation site (Fig. 2). The local persistence of this phenomena is evidence that it plays a part in implantation. Wislocki and Hartman (1929) found the extravasation and bleeding to be limited to the implantation site.

Extravasation of blood, with some bleeding into the uterus, was demonstrated by Evans (1928) in the rat to be dependent solely upon maternal changes and not upon the presence of an embryo. This was possible, since in this animal deciduomas develop spontaneously. Krehbiel (1937) produced deciduomas and found similar extravasation and bleeding. Long and Evans (1920) applied the term "placental sign" to this type of bleeding which occurred frequently during the process of implantation. Corner (1921 and 1923) and Hartman (1932) suggested this vascular phenomenon was for the purpose of supplying blood for the implanted ovum.

Degeneration of maternal tissue in the penetration zone is in part a result of the vascular phenomena described above and in part is due to direct trophoblastic activity in early implantations. Proof of the former is found in the demonstration of the degeneration of tissue in regions remote from trophoblast. Since similar necrosis is demonstrated in endometrium during its cyclic changes, it is concluded that some of the necrosis observed in early pregnancy is a result of vascular phenomena and not dependent entirely upon the activity of the trophoblast.

TROPHOBLASTIC ACTIVITY

In the preceding chapter, it was shown that all the degeneration of maternal tissues in the penetration zone is not due to trophoblastic activity, as believed by most authors, but is due in part to the described vascular phenomena. This seems preferable to the theory of elaboration of ferments by the trophoblast in explaining degeneration of maternal tissue some distance away from fetal elements.

Evidence is present, however, which indicates that the trophoblast has a part in tissue necrosis in the penetration zone. A study of the blood vessels demonstrates fetal trophoblast invading capillary and vein walls (Fig. 3). This invasion is carried out by both individual wandering cells and masses of trophoblast. In many places the walls of the sinuses toward the fetal side are completely destroyed and replaced by trophoblast. The Edwards-Jones-Brewer and the Jones-Brewer I specimens supply multiple evidence of this. That arteries are rarely invaded is explained by the fact that as the arteries approach the penetration zone they rapidly lose their muscular coats

and become capillary structures; whereas in the vera the spiral arteries extend to the surface. The younger specimen demonstrates this clearly. In our specimens there was only one instance found of invasion of an arterial wall.

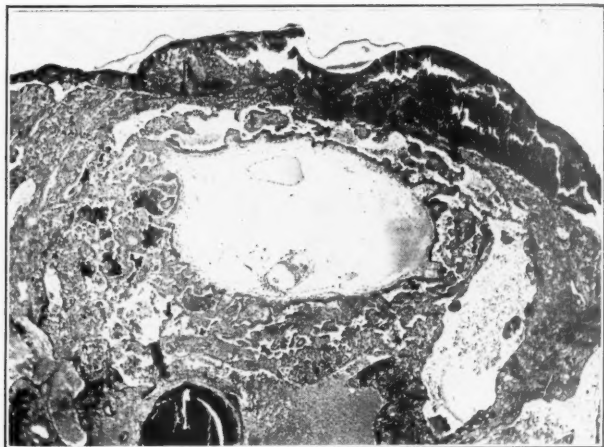


Fig. 3.—The Edwards-Jones-Brewer ovum. The embedded blastocyst in this section is surrounded almost entirely by venous spaces which contain maternal blood. The villi are most numerous on the basal side of the blastocyst. The surface coagulum and depression at the point of entrance are shown in cross-section.



Fig. 4.—The Edwards-Jones-Brewer ovum. About this portion of the endometrial gland which contains blood there are masses of adjacent trophoblast. The gland epithelium is undergoing necrosis and in places is entirely wanting. This photomicrograph demonstrates the active destruction of gland tissue by the trophoblast.

Glands are invaded and their epithelium destroyed by adjacent trophoblast. In this manner blood enters the gland lumen (Fig. 4). That the necrosis of the gland epithelium is a result of the activity

of the adjacent trophoblast is indicated by the fact that only those epithelial cells near the trophoblast are undergoing degenerative changes (Fig. 4).

The reticulum throughout the penetration zone is arranged irregularly in strands and clumps. In places the clumps are thick, broken, and irregular strands surround masses of syncytial cells. These cells lying in the implantation cavity at the junction of maternal tissue have phagocytized strands of reticulum. Destruction of the reticular framework in many places is independent of adjacent trophoblast. It appears evident that the reticulum in many instances has been destroyed and broken up as a result of the superficial ischemia produced by the associated vasoconstriction (Brewer). When partly disintegrated, the strands are phagocytized by the syncytium.

Phagocytosis by the trophoblast is repeatedly noted. Red blood cells, leucocytes, lymphocytes, and reticulum are the most frequent maternal tissues phagocytized. The red blood cells rapidly lose their hemoglobin when ingested. Greenhill demonstrated iron in the fetal wandering cells and the above indicates the source of that iron.

The cytotrophoblastic cells also phagocytize maternal cells, chiefly red blood cells, lymphocytes, and leucocytes.

Glycogen was demonstrated in the fetal wandering cells in the Jones-Brewer I specimen. Presumably the glycogen was obtained from the uterine gland cells since this was the only other cell type in which glycogen could be demonstrated.

EDWARDS-JONES-BREWER OVUM

The Edwards-Jones-Brewer ovum was obtained by abdominal hysterectomy performed for multiple small fibroids and a dermoid cyst of the ovary. There was no abnormality of the menstrual cycle. The history is as follows: Last menstrual period Feb. 15 to Feb. 19, 1935. Period expected but failed to appear March 15, 1935. Operation (hysterectomy) March 20, 1935. The ovum was embedded on the posterior surface of the endometrium. Because of the small size no attempt was made to dissect it out grossly as was done in some of the other specimens.

The embryonic disc was cut in almost a transverse plane (Fig. 5). The body stalk and primitive streak region indicate the axis of the embryo.

The villi are short and not numerous (Figs. 3 and 5). They are more abundant on the basal side of the blastocyst. The syncytium covers the entire surface except the tips of the villi. In the outer portion of the implantation cavity the syncytium is identical to the primary syncytium described by Teacher, Bryce, and Grosser. It has a spun-out arrangement similar to their descriptions. Evidence of vacuolization of the syncytium as described by many workers is not noted to any great extent in this ovum. The formation of syncytium is described in conjunction with the Jones-Brewer I ovum.

Destruction of maternal tissue by the trophoblast is demonstrated. Venous sinuses, glands, and reticulum are the most frequently involved structures.

The embryonic anlage is attached at the most dependent pole of the blastocyst which is almost the universal rule (Fig. 3). The amnion is larger than the yolk sac in this specimen (Fig. 6). There are no blood vessel formations in the embryonic structure.

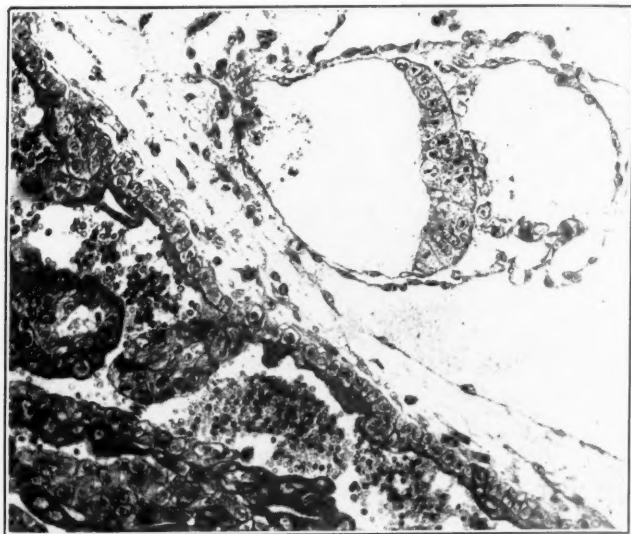


Fig. 5.—The Edwards-Jones-Brewer ovum. The embryonic disc is composed of a single row of columnar cells resting upon a definite basement membrane. The junction of the amnion with the disc is distinct. The amnion is larger than the yolk sac. The mesoblast of the chorionic wall invests the peak of the amnion.

The cells of the yolk sac are flat and elongated in all parts except beneath the disc where the primitive endodermal are cuboidal and are regularly arranged. There are no blood vessel or blood cell formations.



Fig. 6.—The Jones-Brewer ovum I. This photomicrograph of the implantation site shows the embryonic anlage attached at the most dependent pole. The villi are branched. About the blastocyst there are numerous dilated venous sinuses. The uterine glands are tortuous and filled with secretion. In this older specimen there is not as much hemorrhage about the implanted ovum as there is in the younger Edwards-Jones-Brewer and the Peters specimens.

The embryonic disc is flat and has no distinctive surface markings. The most striking feature is the absence of mesoblastic proliferation between the ectodermal plate and the entoderm (Fig. 5). The primitive streak is in the earliest developmental stage yet described for man. At the caudal end of the disc the basement membrane of the disc is disrupted and there is a piling up of the ectodermal and entodermal cells. Cells in mitosis are abundant, indicating a center of intensive growth. Streeter has shown in the pig that such a center is the site of the primitive streak.

The measurements made on the slides and the model are: External chorion 3.6 by 3.0 by 1.9 mm., internal chorion 1.85 by 1.71 by 1.01 mm., embryonic disc 0.209 by 0.177 mm., amnion 0.223 by 0.178 by 0.167 mm., yolk sac 0.197 by 0.160 by 0.120 mm., and greatest length of mesodermal villus 0.27 mm.

In this early specimen the disc is slightly longer than it is wide, while in the older Fitzgerald-Brewer I ovum the disc is circular in outline. This is true although the development and proliferation of a primitive streak in the latter specimen is well advanced. It has been suggested that the growth of tissue from the primitive streak causes elongation of the disc. The evidence obtained in the Edwards-Jones-Brewer, the Jones-Brewer I, and the Fitzgerald-Brewer I ova, however, indicates that the first proliferation of tissue from the streak is lateralward and results at times in a primary broadening of the disc. It is also apparent that there are other factors that account for the various shapes of the discs of very early ova. Streeter pictures variation in shape in young pig ova and the human ova are now shown to be similarly varied.

JONES-BREWER I EMBRYO

This ovum was obtained by vaginal hysterectomy. The operative procedure was a repair of an extensive laceration of the anterior and posterior vaginal walls and perineum. Vaginal hysterectomy was performed because of markedly relaxed uterine supports and a badly lacerated and eroded cervix.

After hospitalization and before operation the patient developed an upper respiratory infection and operation was delayed for fourteen days. During this time the patient, who had remained in the hospital, missed a menstrual period. This fact was not noted at that time. Her previous menstruation was normal. An exact coital history was obtained from both husband and wife.

Last menstrual period began Feb. 16, 1932, and ended Feb. 22, 1932. Coitus Feb. 26, Feb. 28, and March 4, 1932. Entered hospital March 10, 1932. Menstruation expected but failed to occur March 13, 1932. Hysterectomy (thirty-seventh day of cycle) March 24, 1932.

The body of the uterus after removal was 10.5 by 7.5 by 4.5 cm. and was without pathologic changes. The endometrium averaged 1 cm. in thickness. The ovum was embedded on the posterior endometrial surface, and it was depressed beneath the general level of the decidua (Fig. 6). The measurements are as follows: External chorion 8 by 7 by 4 mm., internal chorion 6 by 5 by 2.5 mm., embryonic disc 0.590 by 0.0782 mm., amnion 0.0592 by 0.0805 by 0.026 mm., yolk sac 0.072 by 0.079 by 0.076 mm., and primitive streak.

The blastocyst is covered with branched chorionic villi (Fig. 6). Syncytium composes the outer surface of the chorion and covers all of each villus except the tip. The Langhans cells project out beyond the ends of the villi as cell columns. It is a prevalent conception that these cells develop into syncytium. In the specimens of this report, more evidence is presented in accord with this view. In the Jones-Brewer I ovum the cells near the origin of the cell columns are dividing rapidly by mitotic division. The Langhans cells are also dividing rapidly. Syncytial formation is at a maximum during the stage of active division of these cells. Mitochondria are identical in these cells and in the syncytium. Changes in the amount

and staining qualities of the cytotrophoblast are demonstrated. The amount of granular cytoplasm increases until it is as dense as that of the syncytium. The staining qualities also increase in intensity.

In the Edwards-Jones-Brewer ovum similar changes are noted. Cytotrophoblastic cells are seen fusing together with a loss of cell membranes between them to form a multinucleated cell mass. These masses are in all respects like syncytium. Most of the secondary syncytium possesses a brush border, and numerous cytotrophoblastic cells also are shown to have faint brush borders. The cytotrophoblastic cells have a phagocytic activity similar to that of syncytium.

In addition to following the transitional phases in the formation of syncytium from the Langhans cells and cytotrophoblastic cells, and demonstrating the similar activities of these cell types, there is one phenomenon that strongly enhances this theory of syncytial formation. That is the fact that the Langhans cells disappear early in pregnancy. After disappearance of the Langhans cells syncytial formation

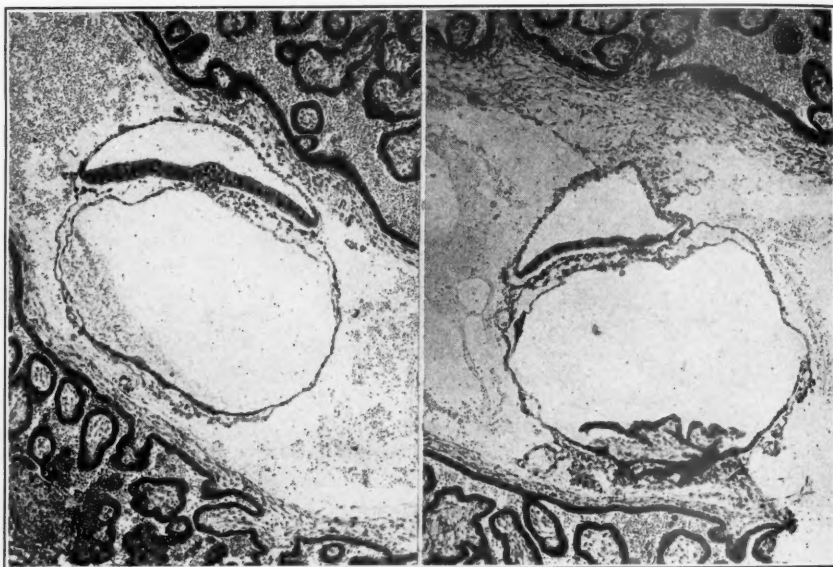


Fig. 7.

Fig. 8.

Fig. 7.—The Jones-Brewer ovum I. This is a photomicrograph of a slightly oblique section through the cephalic part of Hensen's node. The yolk sac is larger than the amnion. The embryonic disc is elevated in the region of Hensen's node. Laterally from the nodal tissue there is a growth of mesoblast between the embryonic plate and entoderm.

Fig. 8.—The Jones-Brewer ovum I. This section pictured is through the primitive streak. There is a distinct primitive groove with elevated parallel ridge. The lateral growth of mesoblast is at a maximum in this section. The streak cells are fused intimately with the ectodermal plate cells. There is no fusion with the entoderm at this point. The body stalk composed of chorionic mesoderm encloses the tip of the amnion.

is rare. This suggests that the Langhans cells have been used up in carrying out their function of forming syncytium.

The embryonic anlage is attached at the most dependent pole of the chorion (Fig. 6). There is a distinct penetration zone or zone of necrosis. Uterine glands, venous sinuses, and stromal tissues have been penetrated and destroyed. Blood vessels in various stages of development were present in the villi, chorionic wall, body stalk, and portions of the wall of the yolk sac. These vessels arise in situ.

The embryonic disc which has both a transverse and cephalo-caudal arching, is slightly broader than it is long. There is a definite Hensen's node (Fig. 7). The

node is located near the center of the disc and is elevated above the surface. The cells comprising the node are arranged in a radial manner about several small slit-like cavities. This cell arrangement extends through to the dorsal surface of the disc but there is no opening demonstrable. This ovum presents the earliest stage in the formation of Hensen's node and neurenteric canal so far described in the human being. There is a primitive streak and groove (Fig. 8), cloacal membrane, and allantois.

FITZGERALD-BREWER I OVUM

This specimen was obtained by abdominal hysterectomy which was performed for the purpose of sterilization because of severe mitral heart disease. The patient had a normal thirty-day menstrual cycle.

Last menstrual period began June 25, 1934. Period expected but failed to appear July 25, 1934. Hysterectomy (thirty-eighth day of cycle) Aug. 2, 1934. An accurate coital history was not obtained.

The uterus was without pathologic changes. The blastocyst was embedded on the posterior wall of the endometrium and was elevated above the general level of

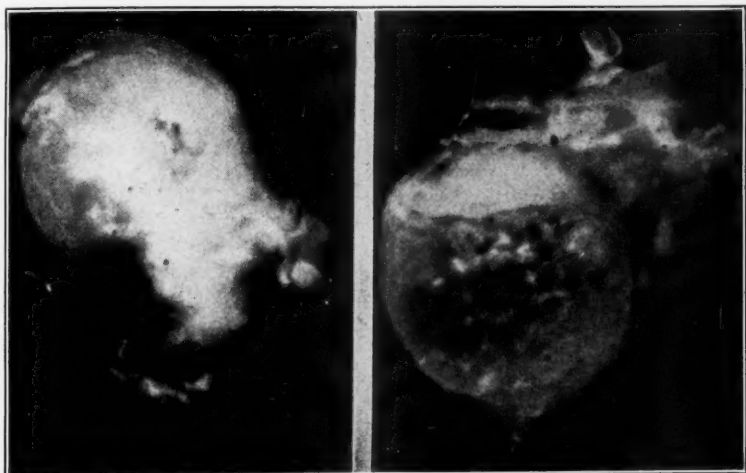


Fig. 9.

Fig. 10.

Fig. 9.—The Fitzgerald-Brewer ovum I. This photograph of the surface of the embryonic disc was taken after the embryonic anlage had been dissected out grossly. The irregular, dense tissue at the lower right is the body stalk. The disc is seen as an opaque structure with a clear-cut circular edge. At the center point there is a more dense region which represents Hensen's node. The yolk sac is the larger circular and less opaque structure.

This photograph was taken through the amnion.

Fig. 10.—The Fitzgerald-Brewer ovum I. This is a lateral view of the embryonic anlage showing the spherical yolk sac on top of which rests the opaque embryonic disc. The cephalocaudal arching of the disc is discernible. The elevation near the center of the disc is Hensen's node. The edge of the disc is quite even and regular.

The amnion is transparent except where the body stalk encloses it.

the decidua. The measurements of the ovum are: External chorion 10 by 9 by 5.5 mm., internal chorion 7 by 6 by 3 mm., embryonic disc 0.88 by 0.84 mm., amnion 0.89 by 0.86 mm., yolk sac 1.2 mm. in diameter, primitive streak including Hensen's node 0.42 mm., and prochordal plate and head process 0.1 mm.

The blastocyst was covered with branched villi. There was destruction of the uterine glands, stromal tissues, and venous sinuses as in the previous specimens. The anlage was similarly attached to the deepest pole of the chorion. There are blood vessel formations in the villi, chorion, body stalk, and yolk sac.

The embryonic disc was dissected out and photographs made (Figs. 9 and 10). From these the disc was oriented and cut in a transverse plane. The embryonic disc, which is circular in outline by geometric projection, has near its center an elevated Hensen's node. The cells of the node are arranged in a similar manner to that noted in the Jones-Brewer I specimen (Fig. 11). The radial arrangement, however, is more complete and extends over a greater distance. There is also more definite canalization.

The head process is in a very early developmental stage. The cells are grouped about a central point or in places about a central cavity or canal. The canalization is incomplete through the short extent of the cordlike head process. The cells of the head process are a direct continuation of the cells of the node. They are smaller than the node cells.

The caudal surface of the disc is interrupted in the midline by a deep primitive groove (Fig. 12). There is a primitive groove, streak, a cloacal membrane, and an allantois. The groove is somewhat tortuous and is deeper than that of the Jones-Brewer I ovum. Photographs of the normal ovum demonstrate the exact contour, size,

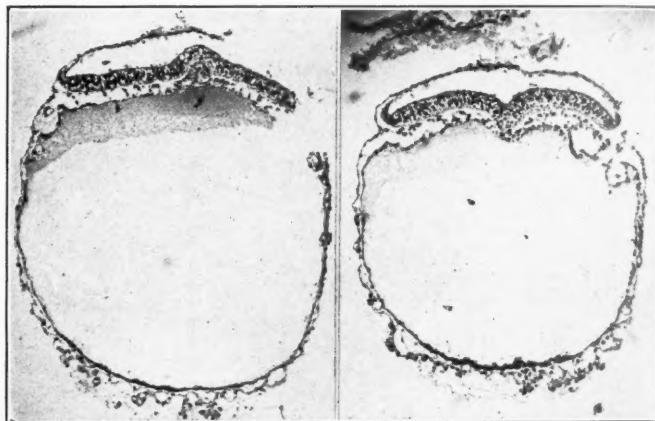


Fig. 11.

Fig. 12.

Fig. 11.—The Fitzgerald-Brewer ovum I. This is a photomicrograph of a section through the mid-portion of Hensen's node. Hensen's node is elevated and is composed of radially arranged cells. At the center point there is a small round cavity which extends cephalward through a few sections. Lateral extension of the mesoblast is slight.

Fig. 12.—The Fitzgerald-Brewer ovum I. This photomicrograph of a section through the caudal part of the disc shows a deep primitive groove with a large primitive streak area. There is extensive lateral growth of the mesoblast.

and axis of the disc. The latter is of value in orienting the specimen and in cutting the serial sections in an exact chosen plane. The slight tear of the yolk sac wall fortunately was of little consequence compared with the great value of obtaining actual photographs of the embryonic disc.

JONES-BREWER II OVUM

The ovum was obtained by hysterectomy done on the forty-ninth day of the menstrual cycle for uterine fibroids. There was no accurate coital history. The blastocyst was embedded on the posterior wall of the uterus, and projected 1 cm. above the general endometrial surface. Measurements made on the slides are: External chorion 12 by 6 mm., internal chorion 9 by 3 mm., embryonic disc 0.74 by 0.60 mm., and yolk sac 1.3 mm.

The blastocyst was completely surrounded by secondary branched villi. The embryonic anlage was serially sectioned in a sagittal plane (Fig. 13). The cut sections were somewhat unequal in thickness. There is a primitive streak with lateral proliferation of the mesoblast, and there is a well-developed head process. The head process does not extend forward far beyond the node and the cells are between the embryonic plate cells and the entoderm. There is only occasional fusion of the head process with the entoderm. Hensen's node is a distinct elevation near the center of the disc. The cells of the head process and node are continuous. Because of the plane of section, a radial arrangement of the cells and a central cavity are not demonstrable. The disc is longer than it is wide. There is a definite allantois and cloacal membrane. The allantois, as in the other ova, is a tortuous structure lined with cuboidal epithelium. The body stalk, yolk sac, and chorionic villi contain definite vascular structures in which there are primitive blood cells. The body stalk is a more advanced structure than that of any of the other specimens described in this paper. Due to the trauma in opening the blastocyst in the fresh state, the body stalk and yolk sac were torn loose. These structures are considerably more advanced in development compared with those of the previously described ova.



Fig. 13.—The Jones-Brewer ovum II. This photomicrograph was made of a sagittal section near the midline of the embryonic disc. Hensen's node region is elevated. The nodal cells are densely grouped and cephalward there extends a loosely arranged column of cells, the head process.

The primitive streak is well developed and in places is fused with the entoderm. The arching of the disc is more abrupt than that of the other specimens of this report.

The body stalk is large and contains vessel formations. In it, also, there is a well-formed allantois. The allantois is seen to extend outward from the yolk sac.

The amnion is smaller than the yolk sac.

FITZGERALD-BREWER II OVUM

The Fitzgerald-Brewer II ovum was also obtained by hysterectomy. The procedure was done for the purpose of sterilization because of severe mitral heart disease. The pregnancy was normal in all respects. The uterus had no pathologic changes.

The patient had a regular thirty-day type of menstrual flow. The flow lasted from three to five days. The last menstrual period began forty-one days before operation.

The measurements made on the gross specimen with the aid of a dissecting microscope are: External chorion 10 by 6.4 mm., internal chorion 7.8 by 4.1 mm., and yolk sac 2.2.

Measured on the photographs and reduced to actual size, the disc is 1.48 by 1.205 mm. The blastocyst is covered with branched villi (Fig. 14). The villi are more numerous and longer on the basal side. The magma within is dense. The embryonic anlage is attached near one side of the chorion.

The anlage was dissected out grossly and the yolk sac was divided in order to obtain a photograph of the intact disc (Fig. 15). Under a dissecting scope the primitive groove and Hensen's node were readily visible. A head process is indicated by a dense opacity in front of the node.

FITZGERALD OVUM

The specimen was obtained by abdominal hysterectomy. The operation was performed because of multiple large fibromyomas. The patient had a normal thirty-day menstrual cycle, and there was no accurate coital history. The hysterectomy was performed on the thirty-fifth day of the cycle.

The uterus was as large as a large grapefruit. It contained many subserous and intramural fibroids. The endometrium was without gross pathologic changes. The blastocyst was embedded on the posterior wall of the endometrium in the fundal area and was definitely elevated above the decidual level. The measurements

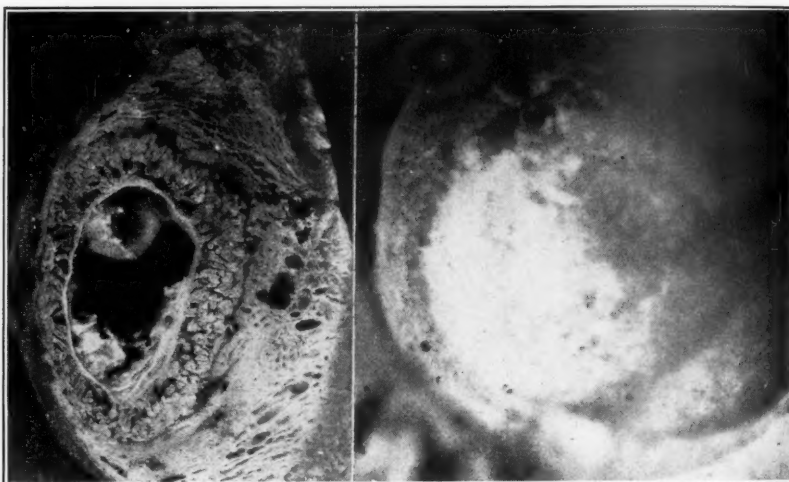


Fig. 14.

Fig. 15.

Fig. 14.—The Fitzgerald-Brewer ovum II. This photograph was made of the embedded blastocyst and embryonic anlage after the blastocyst had been cut away on either side of the anlage.

The villi are branched and completely surround the blastocyst. The magma is dense and is adherent to the yolk sac.

The yolk sac is larger than the amnion. The lateral edge of the disc is seen resting on the yolk sac.

Fig. 15.—The Fitzgerald-Brewer ovum II. Before making this photograph the embryonic anlage, as shown in Fig. 14, was dissected out and the basal half of the yolk sac was cut away. In this manner the more dense embryonic disc was made visible. The shape of the disc is oval with a narrowing in the caudal portion. The border is regular and distinct. Near the central point on the disc there is a still more dense region, the Hensen's node. Forward from this there is a pointed opacity which represents the head process. The primitive streak is suggested but not clearly defined.

of the ovum are: External chorion 14 by 12 by 9 mm., internal chorion 11 by 10.5 by 5 mm., embryonic disc 1.085 by 0.6 mm., amnion 1.1 by 0.7 mm., and yolk sac 1.3 by 1.2 by 1.4 mm.

There was a primitive streak including Hensen's node. The blastocyst was covered with branched villi which were as long as 1 mm. The ovum was sectioned in a plane which deviates but slightly from the longitudinal. All sections

were saved and arranged serially. A complete reconstruction of the embryo was made through the courtesy of Dr. George Streeter, and drawings of the model were made by James F. Didusch.

The embryonic anlage was attached to the deepest pole of the chorion. Blood vessel formation was evident in the villi, body stalk, yolk sac, and chorion. The embryonic disc was pear-shaped in outline. Hensen's node is a distinct and circumscribed elevation near the center of the disc. Extending caudally was a very deep primitive groove. A cordlike head process extended cephally from Hensen's node. There was a cloacal membrane and an allantois. The embryo was in its anatomic development slightly older than the Fitzgerald-Brewer II and the Jones-Brewer II ova. It was of considerable value in that it was perhaps the best preserved presomite embryo sectioned longitudinally, and as evidence of the fact that the shape of the disc may vary greatly in embryos of approximately the same development.

COMPARISON OF OVA

Arrangement of these ova according to age determinations is difficult, since the two most important factors in age determinations, the exact time of ovulation and the time required for fertilization, cannot be ascertained. Because of this, absolute age determinations cannot be made. In the past few years evidence as to the time of ovulation has been presented by various workers, both for the human being and the macaque. On the basis of such data there has been a general acceptance of a so-called "safe period." A study by Brewer of the young presomite human ova with critical data demonstrated that one-half of these young ova had their inception in the "safe period." This indicates that the time of ovulation in the human being is subject to wide variation and that a "safe period" is not entirely trustworthy.

A comparison based on the sizes, shapes, and stages of development is the method by which most ova are chronologically arranged. The size and shape of an embryonic disc are most accurately determined by actual photographs of the intact disc. The Fitzgerald-Brewer I specimen was dissected grossly and the disc photographed from various angles. By geometric projection of the photographs the disc is shown to be round. Although the disc is round there is an early head process formation. From the work which has previously appeared in the literature, one is led to suppose that there is an early elongation of the disc with the development of the primitive streak, Hensen's node, and the head process. In the Fitzgerald-Brewer II ovum actual photographs of the disc demonstrate an elongation of the disc but this elongation is relatively less than that of other reported ova.

Photographic lateral views portray accurately the arching of the embryonic disc and make it possible to obtain accurate measurements over that curve.

Such photographs reveal that variations in shape and size do occur normally.

CONCLUSIONS

1. Six normal and complete presomite human ova are presented.
2. The vascular changes in the endometrium of early pregnancies are similar to those phenomena in the normal menstrual cycle.
3. These changes are vasodilatation and vasoconstriction, extravasation of blood, congestion of the superficial venous sinuses, and necrosis in the superficial portions of the endometrium.
4. These phenomena are primarily for the purpose of preparing a site for implantation of the human ovum.
5. The trophoblastic activity consists of invasion and destruction of maternal capillaries, venous sinuses, glands, reticulum, and stromal cells. Phagocytic activity is also demonstrated by the trophoblast.
6. Actual photographs of embryonic discs show them to vary in size, shape, and stage of development even though they are near the same age.
7. The "safe period" is not completely trustworthy since half of the human ova with critical data and complete descriptions were fertilized during the "safe period."

We wish to express our appreciation for the aid given by Dr. G. W. Barthelmez.

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RETROGRADE CYSTOCELE OPERATION*

A PRELIMINARY REPORT

J. L. BUBIS, M.D., F.A.C.S., CLEVELAND, OHIO

(From the Service of Obstetrics and Gynecology, Mt. Sinai Hospital)

WHEN both an abdominal hysterectomy and a cystocele repair operation are indicated, the usual method is to repair the cystocele per vaginam and then perform a laparotomy for the hysterectomy. In the course of this procedure several of the newly placed important sutures must be cut in order to free the cervix from the vesicouterine ligament and the upper anterior portion of the vagina, thus increasing the danger of hemorrhage and necessitating a duplication of fascial and vaginal suturing. To eliminate these difficulties, I performed on April 4, 1935, a retrograde cystocele operation (Case No. 0-1642, described later). A total hysterectomy was performed first and then through the same abdominal incision a new support for the sagging base of the bladder was made by the repair and restoration of the torn and overstretched pubovesical or uteropubic fascia (George Gray Ward). This operation calls for very careful technic, as the bleeding from the plexus of veins near the urethra is often hard to control, and it is somewhat more difficult to build up a urethral support than by the classical method, but we find that this revision of order has several decided advantages. First, the retrograde cystocele operation eliminates the danger of cutting previously placed sutures. Second, after an abdominal hysterectomy has been performed, the herniation of the bladder is better exposed. Third, the exact position of the ureters can easily be demonstrated. Fourth, after the repair of the fascia by this method, the implantation of the round ligaments on the anterior cuff of the vaginal wall helps give additional support to the bladder. Fifth, there is a slight saving of time.

This report covers a series of twenty retrograde cystocele operations, although five more have since been performed in addition to this number with excellent results. In all these cases, abdominal hysterectomies were definitely indicated. We prefer to do complete hysterectomies unless the cervix is absolutely normal or the patient's condition does not warrant this radical procedure. A retrograde cystocele is best performed when the uterus and cervix have been removed. We did several retrograde cystocele operations after supracervical hysterectomies, but on account of incomplete drainage, this was discontinued.

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Eleven of the cases recorded were private and nine were dispensary patients. The average age was about forty-two years, the youngest was thirty years and the oldest was fifty-one years. Most of the women were para ii or iii, were quite stout, had deep pelves, and a number of them had large pendulous abdomens. Several had had previous operations which complicated the procedures and interfered with the healing of the tissues. Most of these women had severe lacerations of the cervix, all of them had chronic infected cervixes, and in most cases the infection had traveled up through the tubes and along the uterosacral ligaments or along the bases of the broad ligaments, causing chronic pelvic disease (P.I.D.) with adhesions, thus making a clean, dry dissection impossible. Two patients who had marked cystoceles were nulliparas with large fibroids (Cases 0-1642 and 0-4327).

PROCEDURE

Preoperative Treatment.—The majority of patients upon whom a retrograde cystocele operation can be done are over forty years of age and in poor health due to chronic infections of the cervix, or a multiplicity of pathologic conditions in the abdomen, pelvis, and vaginal canal; many are tired or worn out from overwork or excessive loss of blood at the menstrual periods; some suffer from carious teeth and pyorrhea. The importance of getting them in the best possible condition by rest in bed and removal of any known foci of infection can readily be seen. Urinalysis, blood tests and counts, electrocardiographs, and basal metabolism tests should be done if indicated. All patients should be typed for transfusions which are often advisable on account of the extensive operations with their accompanying loss of blood and shock.

On the evening previous to the operation, the vulvae and abdomen are given the usual preparation. The patient is given an antiseptic douche, and a good night's rest is assured by the use of bromides, sedatives, or hypnotic drugs. Before being taken to the operating room she is given a hypodermic injection of $\frac{1}{4}$ gr. of morphine sulphate and $\frac{1}{150}$ gr. of atropine. Until the surgeon is familiar with the technic of this operation, it is advisable to insert ureteral catheters up to the kidney pelves to be removed at the end of the operation. This precedes the anesthetic, which is generally nitrous oxide plus oxygen and ether, administered by expert anesthetists. When inhalation anesthesia is contraindicated, and we think the operation can be completed within an hour and a half, spinal anesthesia is used. After the patient is anesthetized, she is placed in the lithotomy position, the vulvae and thighs are painted with a 2 per cent iodine solution which is washed off thoroughly with 70 per cent alcohol solution. The vagina is treated in the same way, care being taken to cleanse the vaginal fornices. After draping the patient, a Pezzar catheter is inserted into the bladder, the urine is drained off, the catheter is left in situ, and clamped off.

Operative Technic.—The cervix is then inspected, and if it is infected, it is either cauterized with the actual cautery or the cervical canal is dilated and an iodine tape is inserted into the uterine cavity, allowing the end to lie in contact with the cervix. If there is a relaxed perineum, with or without hemorrhoids, the technic described in my book, *Puerperal Gynecology* (Wm. Wood & Co., Baltimore, 1935), is followed.

The patient is then changed to the dorsal posture, and the entire abdomen starting from the pubic region to the breasts and laterally as low as possible is prepared

by the iodine-alcohol or other antiseptic method. The drapes are then arranged exposing only the field of incision. Unless there is a midline incision from a previous operation, we prefer the Pfannenstiel or low transverse incision made at the margin of the pubic hair, through the skin, subcutaneous fat and fasciae. All bleeding points are controlled by plain No. 0 catgut ties. Ochsner clamps are then placed at the edges of the cut fasciae and the lower flap is dissected down to the pubic bone. The upper flap is freed in the midline from the muscles and fascia as high as possible, being careful to avoid the two small ilio-hypogastric nerves and their accompanying blood vessels. The two recti muscles are separated and the peritoneum is incised longitudinally. On account of the low position of the incision great care must be exercised to avoid an incision into the bladder. The patient is then placed in the high Trendelenburg position. A Balfour abdominal retractor is in-

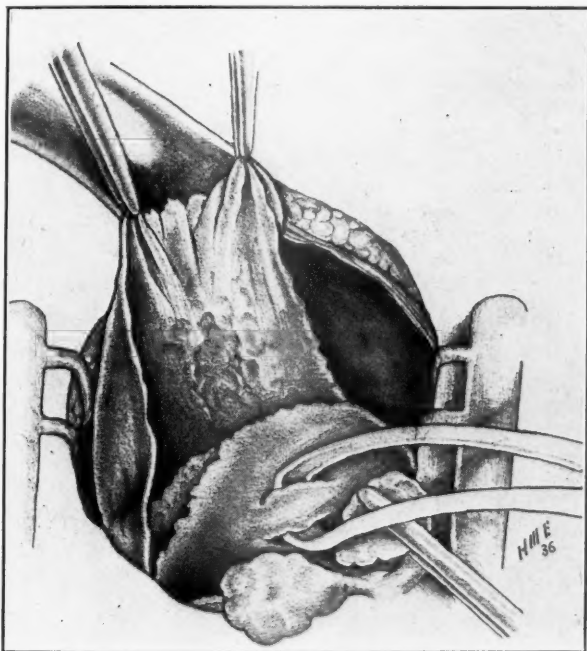


Fig. 1.—Bladder separated from the anterior wall of the uterus.

serted, the pelvis is examined, and a decision is made whether a total hysterectomy alone or with removal of one or more adnexa is to be done. One large gauze pack is so placed that it will be sufficient to keep the abdominal contents out of the pelvis. This is also helped by a wide, flexible ribbon retractor. A large angle retractor placed at the pubic end of the incision helps to give a good exposure. The round ligaments are clamped about an inch from the uterine cornuae, cut and tied. The peritoneum about an inch above the bladder is then incised between the stumps of the round ligaments and dissected down by blunt dissection as far as possible (Fig. 1). The vesicouterine ligament must be incised and the base of the bladder is lifted up and forward by a firm, narrow, ribbon retractor protected by a narrow tape. The broad ligaments are clamped, cut, and tied on both sides down to the isthmus of the uterus. The uterine arteries and their large branches are then cut and tied close to the cervix.

A transverse incision through the peritoneum posteriorly just above the uterosacral ligaments is then made and the flap is pushed downward. The uterus is now pulled up as high as possible and the cervix is palpated through the vaginal walls. An incision is then made through the anterior vaginal fornix, the cervix is grasped with a bullet forceps and pulled upward. The incision is then carried completely around the cervix until the uterus can be removed. All bleeders are clamped, care being taken to include the vaginal mucosa and the adjacent peritoneum, especially laterally and posteriorly. The upper part of the vaginal canal is then wiped dry from above and repainted with a 2 per cent iodine solution. A running interlocking No. 1 chromic catgut suture replaces the clamps (inset on Fig. 2). A clean abdominal pack is then inserted, and the anterior tape which held the bladder out of the way is removed. The anterior peritoneal flap is grasped by several Ochsner clamps, as is the margin of the anterior vaginal cuff (Fig. 3).

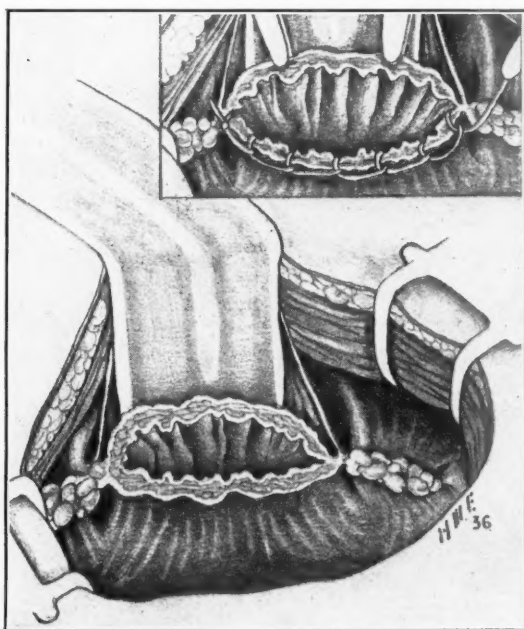


Fig. 2.—Broad and round ligaments cut and tied. The bladder is held back by a narrow retractor. Inset shows the bladder held back by a narrow retractor, two clamps on the edge of the pubovesical fascia, the anterior vaginal wall and a continuous interlocking suture connecting the margins of the posterior vaginal cuff with the peritoneum.

The bladder is then carefully separated from the remains of the pubovesical fascia down toward the urethra until the Pezzar catheter can be palpated. The bladder is held out of the way by a firm, narrow ribbon or Deaver retractor and the fascia is stripped away from the anterior vaginal wall. The fascia may be a thick overstretched sheet of tissue, it may have a hernial pouch in the center with firm edges (so-called Pillars of the Bladder), or it may be very thin, ragged and torn down through the center to the urethra (Fig. 4).

The difficulty encountered in separating the bladder from the fascia and the latter from the vaginal wall depends on the thickness and strength of the remains of the fascia, on the success of getting the lines of cleavage, and on the amount of scar tissue present. The ureters are practically always out of the way if the

right technic is used, although we have occasionally exposed them for anatomic study without any serious after effects. (Cases 0-5014, 0-5446, 0-4327, 0-3809, 0-3872.) The ureters may be kinked or caught in the sutures when the uterus is pulled high in the pelvis (Fig. 5, *B*), when the uterine arteries are clamped and

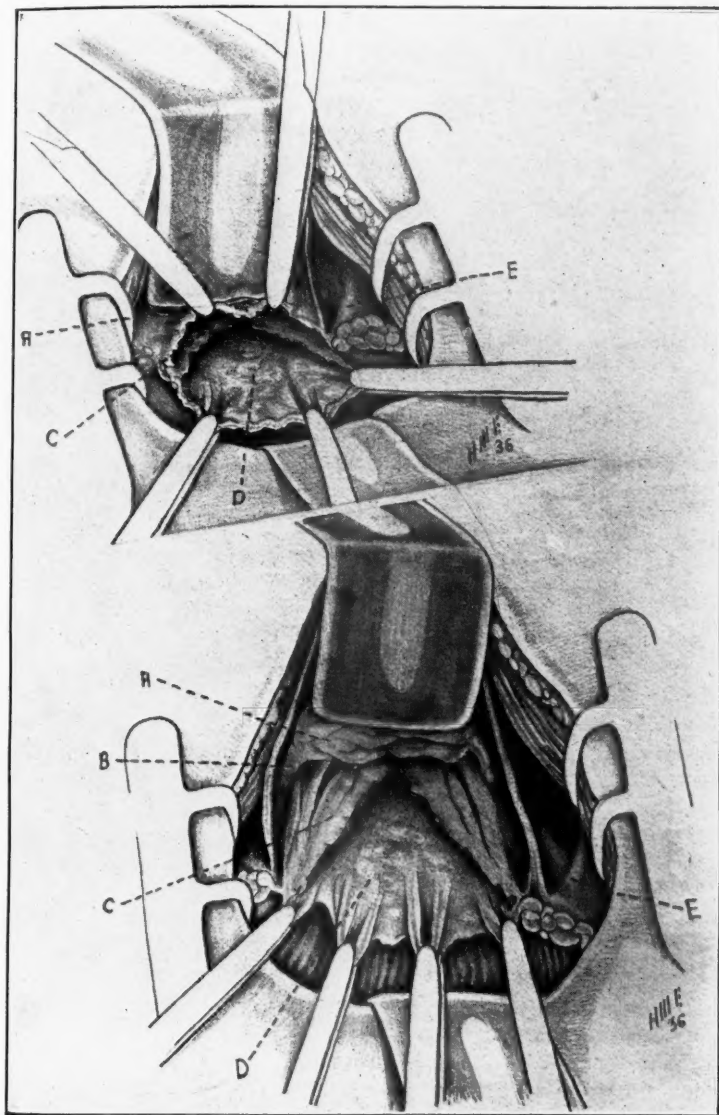


Fig. 3.—*A* is the base of the bladder. *B* is the left ureter. *C* shows the remains of the pubovesical fascia. *D* is the anterior vaginal wall. *E* is the right round ligament.

tied, or they may become closed by edema and swelling of the surrounding tissues, thus causing signs and symptoms of acute urinary retention (No. P-2078).

The next step is the most difficult part of the procedure. This is the reconstruction of the pubovesical fascia, with either interrupted or continuous No. 2 catgut

sutures on small Bubis needles, starting as low toward the urethra as possible and working upward toward the abdominal incision, incorporating a small amount of bladder, vagina, or both tissues in the sutures (Fig. 6). This helps to control oozing and bleeding points and obliterates any "dead" spaces. After the new support for

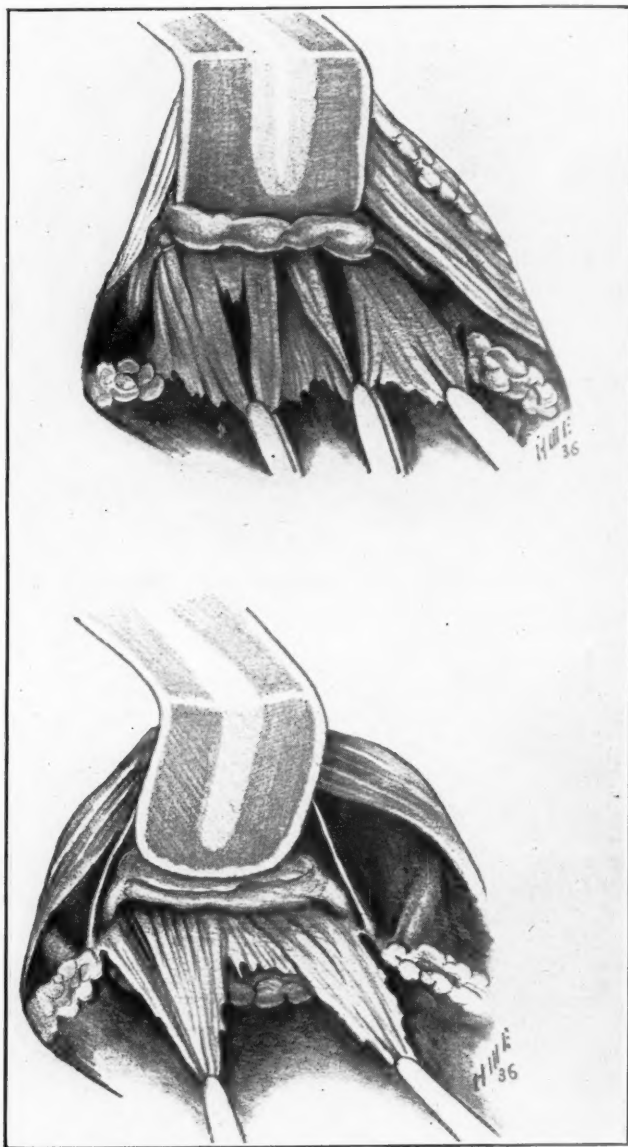


Fig. 4.—Two of the types of fascial remains encountered in our series.

the bladder has been finished, the slack of the anterior vaginal wall is taken up by tension on the Ochsner clamps attached to its edge and two or more plain catgut sutures obliterate the space between the vagina and the bladder, or a wedge-shaped excision may be made with the base toward the abdominal incision. The two edges

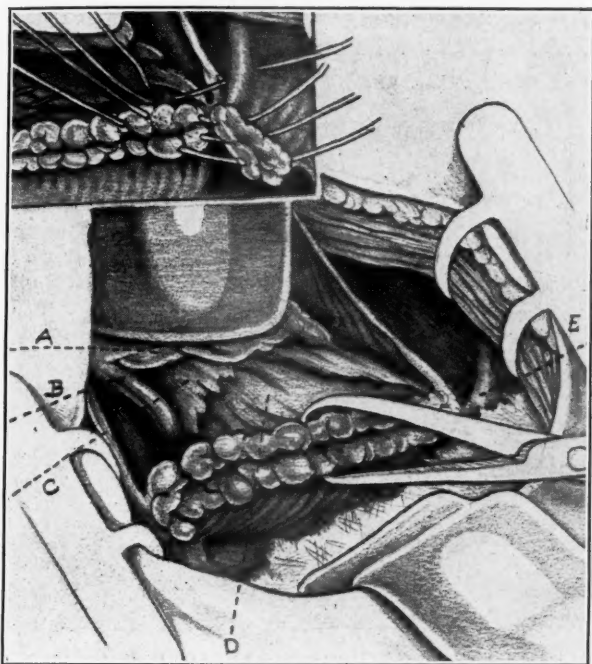


Fig. 5.—Same as Fig. 3. *Inset.* Shows coaptation of the right broad ligament stump and a suture on the round ligament which is pulled over the upper portion of the anterior vaginal thus preventing procidentia of the vagina.

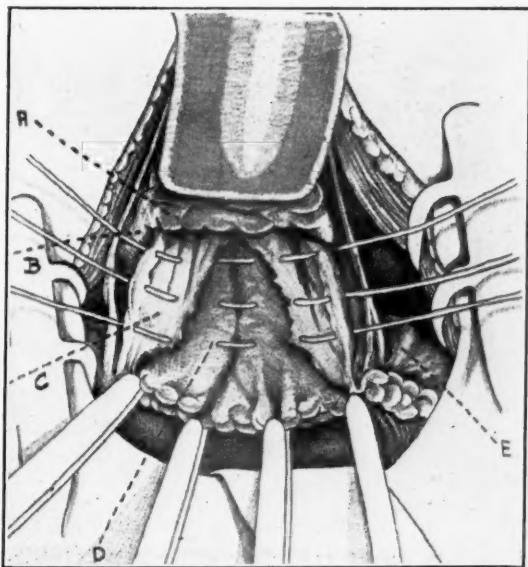


Fig. 6.—Sutures placed through the so-called pillars of the bladder, grasping the anterior vaginal wall.

are then brought together in the midline by an interlocking continuous or interrupted No. 1 chromic catgut suture. The upper part of the vaginal canal is left open, although the angles are coapted by sutures (Fig. 5, inset). A large Penrose or cigaret drain may be inserted into the vagina and the abdominal end is placed in the perivesical spaces or carried down into the culdesac. This is removed within a week per vaginam. We have not formed any definite conclusions as to whether patients have a better recovery with or without drains.

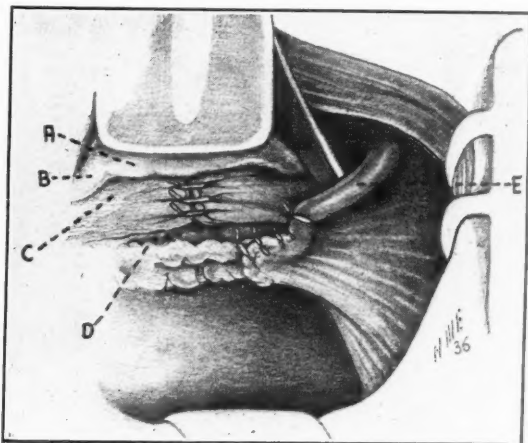


Fig. 7.—A is the bladder. B is the left ureter. C is the reconstructed pubovesical fascia. D is the anterior vaginal cuff. E shows the right round ligament attached to the fascia and the anterior vaginal cuff. We now attach the round ligament to the vaginal wall only.

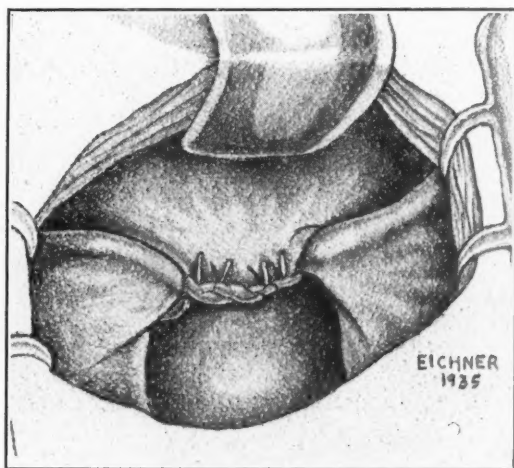


Fig. 8.—Shows the anterior peritoneal flap with the attached bladder sewed to the uterosacral ligaments, covering the vaginal orifice and all raw surfaces.

An important step in the success of the operation is the suturing of the round ligaments to the anterior cuff of the vagina not to the fascial plane as in Fig. 7. This helps to keep the anterior vaginal wall taut, gives added support to the bladder, and prevents future procidentia of the vaginal wall. The anterior peritoneal flap with the attached bladder is then sewed over the vaginal orifice to the uterosacral

ligaments (Fig. 8). At each angle a circular invaginating suture is placed which grasps the vesical peritoneum, the round ligaments, the stump of the infundibulopelvic ligament, the posterior broad ligament, the uterosacral ligament and is brought out through the vesical peritoneum. The parietal peritoneum and the rest of the abdominal incision is closed in layers. The ureteral catheters are then removed but the Pezzar catheter is left in situ for two to six days. Before the patient leaves the operating room she is given 90 per cent oxygen with 10 per cent carbon dioxide inhalations for about two minutes. This stimulates deep breathing and has materially decreased postoperative lung complications.

Inasmuch as all of these women were subjected to prolonged anesthesia and to a multiplicity of operative maneuvers due to marked pathologic changes in the genital tract and reproductive organs, it is very important to work rapidly with as little trauma and loss of blood as possible. The longest time of anesthesia was two hours and forty minutes while the shortest time was one hour and twenty-five minutes, with an average time for the series of two hours and five minutes. The longest time of the abdominal operation was two hours, the shortest one hour, and the average time of abdominal operations in the series was one hour and twenty-nine minutes. Following the operation, if the patient shows signs of shock, she is transfused with 500 to 700 c.c. of whole blood immediately.

In order to demonstrate extreme cases, a brief résumé of two operations follows, one of which entailed the longest and the other the shortest anesthesia.

CASE REPORTS

Mrs. R. G., aged forty-five years, para v, was admitted to the hospital July 30, 1935, complaining of pain in the lower abdomen, burning frequent micturition, and irregular and profuse menstruation. Examination showed a very marked cystocele, rectocele, and a moderate urethral prolapse, a large hypertrophied and infected cervix, and a large boggy uterus. On account of her obesity she was kept in bed and given 5 gr. of desiccated thyroid extract twice daily until her operation on August 3. The procedure followed was: vaginal preparation, insertion of a Pezzar catheter, repair of a rectocele, a change from the lithotomy position, an abdominal preparation, a lipectomy, panhysterectomy, retrograde cystocele repair, appendectomy, and abdominal closure. There was considerable bleeding from the bladder base. The total anesthesia was two hours and forty minutes, with abdominal operation time of two hours. The pulse at the beginning of the operation was 100 beats per minute, which decreased to 85 beats per minute at the end of the operation. At 1:30 P.M., two hours after the operation, her blood pressure was 82/56. She was then given 750 c.c. of 2½ per cent glucose solution intravenously. At 2:30 P.M. the blood pressure was 92/87. She was transfused with 750 c.c. of whole blood by the Kempton Brown method at 8:00 P.M. The following day her blood pressure was 108/78 and gradually rose to normal. On August 5 she had a cough and coarse râles in her chest. She was given 50 c.c. of 20 per cent glucose intravenously. Her temperature rose to 102° F. on this date, and gradually decreased to 99.6° F. on August 10. The Pezzar catheter had been removed on August 8. She complained of urinary frequency for several days, and many bacteria were found in the urine. She left the hospital August 18, fifteen days after the operation, with perfect operative results.

The shortest anesthesia was given in the case of Mrs. G. B. (Case O-1462), aged forty-three years, who was admitted to the hospital April 4, 1935, complaining of leucorrhea, urinary frequency, nocturia, backache, and increased menstruation. She had had three miscarriages, up to six months. She also gave a history very suggestive of an old gonorrheal infection. Examination showed a moderate cystocele

and a fixed fibroid uterus extending to within 3 fingerbreadths of the umbilicus. The operation consisted of a vaginal preparation, a panhysterectomy (both tubes showed marked hydrosalpinx and were matted together with the ovaries), and a retrograde cystocele operation. A cigaret drain was placed in the culdesac and the other end was inserted in the vagina. The appendix was then taken out. Total anesthesia was eighty-five minutes. She developed a wound infection which had to be probed, and Dakin's tubes were inserted. She left the hospital twenty-one days after the operation, the wound well healed, and the urethra well up under the pubic arch.

POSTOPERATIVE TREATMENT

When the patient is returned to her bed, the foot of which is elevated, she is given an intravenous and subcutaneous infusion of glucose and saline solution, her blood pressure and pulse are taken every half hour, and she is watched for vaginal bleeding. Pain and restlessness are controlled by morphine or other sedatives and hypnotics; carbon dioxide and oxygen inhalations, change of posture or position, or intravenous injections of 20 per cent glucose solution are given for respiratory complications. Gastric lavage or gastric decompression by the Levine tube for a dilated stomach, pitressin or other intestinal stimulants, medicated enemas and hot stupes are helpful in the control of intestinal distention. The bladder is drained continually during the first twenty-four hours, and then the Pezzar catheter is clamped and the urine is drained off every two to six hours, followed by an instillation of 2 ounces of 1:4000 neutral acriflavine solution or 1 ounce of 10 per cent argyrol solution. The patient is given some urinary antiseptic by mouth until the catheter is removed or until the urine becomes normal. Tonics, fresh air, mild cathartics, increase in diet, etc., are given as indicated. The general condition of the patient determines the length of the stay in the hospital. The longest number of days was thirty-four, and the shortest number of days was twelve, with an average stay in the hospital of 18.55 days for this series.

COMPLICATIONS

If careful attention is given to the operative technic in gently separating the tissues and controlling hemorrhage, the number and type of complications should not be any greater than those following a total hysterectomy alone. There is a possibility of damage to the bladder unless extreme care is exercised. The following illustrates a case in which difficulty was encountered due to an accumulation of perivesical exudate and edema, and kinking of the ureter. Mrs. R. D., No. P-2078, dispensary patient, aged thirty years, para ii, admitted to the hospital May 5, 1936, complained of pain in the lower abdomen, low backache, leucorrhea, frequent burning micturition, and a protrusion from the vagina. Following the birth of her first child, seven years before, she had had a repair of the cystocele, a partial amputation of the cervix, left salpingo-oophorectomy, and appendectomy. Three years later, her second child was born.

Examination on entrance to the hospital showed a marked cystocele, a lacerated infected cervix extending to the fornices. The uterus was in a retroverted position and adherent. On May 6, 1936, separation of adhesions, a total hysterectomy and retrograde cystocele operation were performed. Much difficulty was encountered due to old scar formation from the previous operation and the inflammation of the bases of the broad ligaments. The length of anesthesia was one hour and forty minutes, and the time of operation was one hour and twenty minutes. She was returned to her room in good condition. On May 10 she complained of pain in the right kidney region and the temperature rose to 102° F. Her condition remained

about the same for several days, and on May 14, one week following operation, Dr. Wm. Rosenberg cystoscoped her and made the following notation: "Bladder urine slightly cloudy and purulent. The bladder capacity is slightly decreased and the patient does not tolerate distention on account of bladder spasm. There is a general cystitis present with numerous flakes or pus and bloody mucus. There is no evidence of diverticulum, but there is a marked deformity of the base of the bladder and the anterior vesicle wall due to the operation. The ureteral orifices are somewhat more lateral than normal, and there is a moderate amount of injection around the left ureteral orifice. The right ureteral orifice is edematous and an impassable obstruction was met 2 cm. above." A retrograde pyelography was done the next day which showed the dye in the left kidney, ureter and bladder, and an obstruction was noted in the right ureter near the bladder. On May 16 there was a profuse sanguineous purulent vaginal discharge. The urine showed 2-plus albumin. On May 20, the urine was much clearer with a moderate number of pus shreds present. Cystoscopic examination showed a mild general cystitis. The deformity noted above had disappeared and the bladder was practically normal in outline. Catheters were passed up both ureters without difficulty. A right pyelogram showed normal filling of kidney, pelvis, and calyces. Slight dilatation of the entire right ureter was present. The upper part of the ureter showed a slight angulation and kinking with apparently no interference with drainage. Two months later she was in good condition, her urinary symptoms had cleared up but examination showed that the anterior wall was slightly sagging.

END-RESULTS

A series of perfect results from any type of cystocele operation is never obtained. There are so many factors involved in the correction and healing of diseased or overstretched tissues in a potentially infected field that any improvement in the comfort of the patient and restitution of the structures to a condition as nearly normal as possible is all that we can hope to obtain.

In this series of twenty cases 14 showed perfect results and 6 showed very marked improvement over their previous condition, three months to a year after the operation.

CONCLUSIONS

1. This operation was devised for those patients who have cystoceles and pelvic pathologic conditions in which total abdominal hysterectomies are indicated.
2. Careful technic, proper lighting facilities, and good assistants are very important.
3. Ureteral catheters are good guides until one is familiar with the landmarks and the technic of the operation.
4. A retention Pezzar catheter also helps to outline the urethra and the adjacent portion of the bladder.
5. Implantation of the round ligaments into the cuff of the anterior vaginal wall beneath the bladder helps to lift the anterior vaginal wall and give added support to the bladder.
6. Restitution of the pubovesical fascia by the abdominal approach eliminates the danger of cutting previously placed sutures and has been proved feasible in the retrograde cystocele operation.

DISCUSSION

DR. CARL P. HUBER, CHICAGO, ILL.—In the literature dealing with the repair of cystocele there are numerous procedures described which have as their distinguishing characteristic an abdominal approach to the bladder area.

The first of these operations was described by Byford in 1890. He operated through the inguinal canals and fastened the tissue on either side of the bladder in the inguinal wounds. Lowson in 1898 reported a procedure in which the bladder is mobilized and pulled upward where it is sutured in approximation to the anterior abdominal wall by a flap of peritoneum containing the urachus and the obliterated hypogastric arteries. Dickinson in 1903 suspended the bladder, usually with the uterus, by actually fixing it to the rectus muscle and fascia.

William Polk in 1909 first described an operation in which the bladder was separated from the uterus and the dissection carried down the anterior vaginal wall to the urethra. The anterior vaginal wall and the fascia under the bladder were then plicated. The operation also included shortening of the round ligaments, while the sacro-uterine ligaments were pulled forward to the anterior portion of the cervical stump. He emphasizes the dangers inherent in the procedure of traumatizing the bladder wall and ureters. In 1921, Lillian Farrar described a similar procedure which she combined with abdominal hysterectomy. The abdominal operation was preceded by any necessary repair of the posterior vaginal wall and cervix. Following these, a supravaginal hysterectomy is performed, the bladder separated from the anterior wall and fastened on a shelf produced by the sutured cervical stump, broad ligaments, round ligaments, and sacrouterine ligaments.

The speaker today offers an admirable description of an operative procedure which technically appears more difficult than a combined vaginal plastic and abdominal hysterectomy. In the absence of personal experience with the particular procedure there are some questions which come to mind before we can wholeheartedly endorse the operation.

1. Is there really an advantage to the procedure over that of the usual combined vaginal and abdominal approach? Technically it seems to me that the advantage is with the combined approach, for certainly the visualization of the operative field is better, and if care is used in placing the sutures from below, I do not believe that there is serious danger of subsequently cutting them.

2. Do improved results warrant a procedure which is more difficult? The author reports 14 cases with perfect results and six cases which showed marked improvement. This surely is commendable, but I do not believe it is superior to the results of vaginal repair. In a series of 100 cystocele repairs reported from the University of Michigan by Norman F. Miller in 1928, there were 94 patients who were cured or definitely improved, 72 of these were reported as completely cured. Incidentally, in this group coincident hysterectomy was indicated in only eight cases. Six were cured and two definitely improved following the operation.

In conclusion, I wish to state that I do not pretend to condemn a procedure without giving it a fair trial. On the other hand, I do not wish to recommend it without due consideration of its merits. I believe that Dr. Bubis should be congratulated upon his attempt to stimulate this plan of attack, but suggest, however, that because of its character this procedure will be limited in its application and should only be attempted by one skilled in pelvic surgery.

DR. BUBIS (closing).—This operation is not intended for all cystoceles. After doing a cystocele repair from below and then going in above to take out the uterus, I have inadvertently cut some of the sutures which I had originally placed. It may be very difficult under these circumstances to control the bleeding and the re-suturing of the upper part of the vagina.

This operation is an anatomic reconstruction of the main support of the bladder, that is, the reconstruction of the pubovesical fascia with the additional support to the bladder by the implantation of the round ligaments into the anterior vaginal cuff under the bladder, which also helps to stretch the vaginal tube.

We are very careful when we say we have a cured case. If there is any deviation from the normal anatomic structure, we call it a failure. Without a strict use of this word we might include several cases in which the patients are in good condition without any sagging.

SOME LESS GENERALLY RECOGNIZED ASPECTS OF GYNECOLOGIC ENDOCRINOLOGY*

EMIL NOVAK, M.D., BALTIMORE, MD.

(From the Gynecological Department, Johns Hopkins Medical School)

THE prime function of the ovary is the production of ova. In spite of the all-importance of this function from a racial standpoint, the ovary is not at all essential to the life of the individual woman. On the other hand, the removal of other endocrine glands whose function seems racially less fundamental, such as the adrenal or hypophysis, is incompatible with life. Profound metabolic disturbances follow the ablation of the thyroid, parathyroid, adrenal, or the hypophysis, while ovariectomy at any epoch of life produces much less striking effects upon the body economy.

Around the relatively simple, or at any rate, readily comprehensible, function of ovulation, there has been an evolutionary building-up of an intricate ancillary mechanism whose purpose is the preparation, extrusion, transport and fertilization of the egg. This mechanism is chiefly of endocrine nature, and is responsible for the intricate phenomena of the reproductive cycle. Teleologically, however, these cyclic phenomena revolve about the reproductive function, so that, from this broad standpoint, even those who no longer accept the doctrine of the "primacy of the ovum" in explaining the rhythm of menstruation will scarcely question the central importance of the egg in the phenomena of the cycle.

Before an audience of trained gynecologists and obstetricians, it is scarcely necessary to discuss the simpler aspects of the endocrinology of the cycle, though many questions are still not clear. There are few gynecologists now who are not familiar with such elementary facts as the following: (1) the rôles played by the follicle and the corpus luteum in the building-up of the endometrium from the end of one cycle to the beginning of the next; (2) the fact that these effects are due to the sequential action of estrin (folliculin) and progesterone; (3) the chronological relations of menstruation and ovulation; (4) the dependence of ovarian function upon that of the hypophysis, through the agency of the

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two pituitary gonadotropic hormones (follicle-ripening and luteinizing); (5) the significance of the anterior pituitary-like principles (prolan) found in the urine of pregnant women; (6) the chief indications and the limitations of organotherapy. To say that we know all about these subjects would be absurd, for most of them are still the subjects of active study and lively discussion. And yet it may fairly be said that we have a good working concept of reproductive endocrinology, lending itself readily to the additions and corrections which each year will bring.

My purpose today is to discuss, along rather broad lines, some aberrations of this normal function, more particularly a few which have not received as much attention in the literature as their interest or importance would seem to justify. Things may go wrong with the ovary from the earliest stages of its development. The zygote is always bisexual, and whether a gonad is to develop into an ovary, a testis, or an ovariostestis is dependent upon the genic balance of the zygote. At its very origin, therefore, gonadal development receives an initial impulse and direction from certain uncontrollable chromosomal factors, and it is this primitive impulse, colored in various ways by the later unfolding of endocrine forces, which must be invoked in the explanation of so many cases of intersexuality. In the differentiating processes of early life, there is every reason to believe that the motivating force is not of endocrine nature, and that segmentation and differentiation proceed according to a foreordained pattern because of some germ-cell force which, for the present, is as mysterious as the life principle, and which might indeed almost be considered the life principle itself. Any one who has seen moving-picture films of the dividing rabbit egg must have been impressed with the remarkable precision with which each new cell falls into its appointed place, just as football players do when the signal is flashed.

x Attractive as it would be to explain the early development of the uterus on the basis of endocrines, there is no evidence to substantiate this view, and it seems likely that early genital development and differentiation are not different from that of other organs and tissues. Even in its undeveloped form, however, the uterus, as well as the mammary gland, already possesses a remarkable sensitivity to endocrine influence, as indicated by the fact that maternal hormones bring about an increase in the size of the uterus so that it is larger at birth than it is shortly afterward, that the withdrawal of these hormones may actually bring about a single pseudomenstrual bleeding a week or so after birth (non-menstrual genital hemorrhage of the newborn), and that mammary growth and even lactation may appear in either the male or female child.

x We know very little, too, about the possible endocrine importance of the ovary in the prepubertal years, though we do know that follicles mature to certain stages of development and that at least some estrin is produced a long while, even several years, before the actual occurrence

of puberty, and that this apparently parallels a similar awakening of pituitary gonadotropic function. It is of interest, too, to note that even in these early postnatal years, the uterus, like the fetal organ, has already acquired its selective responsiveness to the ovarian hormones, as have the breast and other secondary sex organs. This is well illustrated by the occurrence of precocious puberty and menstruation in children as a result of granulosa-cell carcinoma, as well as by the pubertal epithelial hypertrophy of the vaginal mucosa following the administration of estrogenic substances, as in the treatment of gonorrheal vaginitis.

There are still other pathologic departures that may have their origin in these early stages of ovarian development. I have already mentioned the hyperfeminization effects of granulosa-cell carcinoma, which may develop at any age, and which arises from rests of redundant granulosa left over in the early development of the oophorogenic apparatus of the ovary. In the same way, a persistence of cells of masculine proclivity, dating from the masculine scaffolding which precedes the formation of the follicular apparatus, explains the later development of the masculinizing tumors now known as arrhenoblastomas.

It seems to be true, therefore, that the initial germinal impulse is responsible for the original direction of sex differentiation, but that, as the gonads begin to function, they take over the chief burden in unfolding the secondary sex characters of the individual. While we know pathetically little about the mechanism and interrelationship of these two factors, the mere knowledge that the secondary sex phenomena are due to their interplay, and that in the human being as well as in the lower animal varying degrees of sex-reversal may occur, will enable the gynecologist to interpret his cases of intersexuality less unintelligently and less mechanistically than he might do otherwise.

He can appreciate the fact that individuals with testes may, both anatomically and psychologically, be dominantly feminine, and that others with ovaries may have many masculine characters and perhaps dominantly masculine external genitalia. He will, in short, appreciate the fact that the character of the gonad is not the only criterion in sex classification, but that chromosomal factors, with effects depending upon the embryonic age at which they become operative, are usually of much greater importance in determining sex characters. On the other hand, he can likewise appreciate why certain acquired intersexual phenomena may be explainable on a more purely endocrine basis, as in the case of cortical tumors of the adrenal or the group of sex-influencing ovarian tumors mentioned above.

Little as we know of the prepubertal function of the gonads, we do know that it must be of importance, chiefly on the basis of the negative evidence furnished by castration in early life. Observations on the female are exceedingly rare, but they indicate that the operation is followed not only by the failure of appearance of menstruation, but also of

mammary growth and other secondary sex characters, together with a disproportionate skeletal growth like that which so characteristically follows early male castration.

As we approach puberty, the picture of the endocrine function of the ovary begins to stand out more clearly. Long before the first menstruation, maturation of follicles and production of estrin are noted, on the basis of both histologic and hormone studies. The usual sequence of events seems to be, first, incomplete maturation, then complete or almost complete maturation without ovulation but possibly with periodic bleeding, and finally full maturation, with ovulation followed by luteinization and the beginning of the usual ovulatory type of menstruation. It is as if a child, inflating a toy balloon, blows it to larger and larger size with each breath, until finally it bursts. There are certainly, however, individual time variations in the sequence of events outlined above. There can be little doubt, for example, that in many girls, ovulation begins at about the same time as menstruation, or even before, for how else could we explain the numerous cases in which pregnancy is reported to have followed immediately after the onset of the first menses, and those in which pregnancy has occurred before the first menstruation? The evidence indicates, however, that this is certainly not the invariable rule.

It can readily be shown in monkeys, for example, that anovulatory cycles are very frequent, and there is almost equally good evidence in the case of the human being. A purely follicular, anovulatory type of menstruation can be readily determined by the examination of the endometrium. In such cases the menstrual bleeding may be quite normal in amount and fairly regular in rhythm, but often there are irregularities of either amount or tempo of the flow, so that clinically such cases may present themselves as instances of functional bleeding of mild or severe grade, as the case may be.

I shall not here stop to argue the question of whether anovulatory bleeding should be included under the term menstruation, a question which has divided gynecologists into two camps, one holding that menstruation is to be defined merely as a periodic physiologic uterine bleeding, the other that it is to be limited to those cases in which ovulation occurs, a corpus luteum is formed, and certain pregravid endometrial changes thus brought about. I may emphasize, however, that the term menstruation had been used for many hundreds of years before the phenomenon was in any way linked up with pregnancy, and certainly long before the human egg or corpus luteum was discovered. Both the lay and medical concept has always been that of a normal periodic loss of blood from the genital tract, and it would seem to me illogical and unwarranted to add to this original concept the corollary that the term should be limited only to that group of cases in which ovulation occurs, even granting that this is overwhelmingly the most common type.

That ovulation often begins a considerable time after the onset of the menstrual function is indicated also by the clinical observation of what might be called a physiologic sterility in child brides, as has been noted in those of India. The most recent and most complete study of this sort is that of Mikulicz-Radecki and Kausch,¹ who studied a large series of young primigravidas in the Berlin Frauenklinik from the standpoint of their cohabitational histories as related to their fecundity. In a surprisingly large proportion, even though there had been an active sex life from puberty, pregnancy did not occur for from one to several years later. The obvious explanation would seem to be that the menstrual cycles for a variable though perhaps considerable time after puberty may be of the anovulatory type.

To jump to the other extreme of menstrual life, there is no doubt that in a not inconsiderable number of women approaching the menopausal age, sterility occurs because ovulation has ceased even though menstruation still proceeds, perhaps quite normally, perhaps with varying degrees of excess or irregularity, representing one grade or another of functional menorrhagia. That this is true I have been able to convince myself by endometrial biopsy studies in sterile women at this age. In other words, the age incidence of the anovulatory cycle is the same as that of the follicular type of functional bleeding, which is not surprising, since the mechanism of the two is the same, except for degree. In the distinctly abnormal cases of bleeding, the follicle not only fails to rupture, but persists abnormally long, with hyperestrinism as a result. Just as functional hemorrhage may occur at any age during reproductive life, so may the anovulatory cycle, unaccompanied by abnormal bleeding. In the detection of these cases, histologic study of the endometrium obtained just before menstruation, and usually by aspiration-curettage without anesthesia, is of crucial importance.

The question naturally arising is as to whether or not anything can be done about such cases even when they are sifted out. Unfortunately not much in the present state of our knowledge, and chiefly because we know comparatively little of the endocrine factors concerned in ovulation, though obviously they are of pituitary origin. Some believe the follicle-ripening factor the important one in ovulation, some the luteinizing factor. But the investigations of the past year or two, especially those of Hisaw and his coworkers, seem to have established that ovulation is due to neither of these factors alone, but to a delicate quantitative balance between the two. By varying the proportions of these two gonadotropic elements, these investigators have been able to induce ovulation in non-ovulating monkeys.

Unfortunately, however, it seems quite certain that the quantitative balance differs in different species, and, even more unfortunately, in different individuals of the same species, so that, from a clinical standpoint, we are faced with at least a temporary impasse in our management

of these cases. For the present, most of us probably content ourselves with the administration of either the anterior pituitary gonadotropic preparations or prolan substances at or near the usual time of ovulation. In one or two recent anovulatory cases receiving this treatment, a subsequent endometrial biopsy showed an undoubtedly secretory endometrium, indicating that ovulation had occurred. This evidence, however, is far from convincing, as women, like monkeys, may ovulate with some cycles and not with others.

To pass to another type of ovarian dysfunction, amenorrhea furnishes a good illustration of the multiplicity of factors which may operate to bring about the same clinical symptom, emphasizing the absurdity of the old rule-of-thumb plans of treating menstrual disorders. The three endocrine glands most frequently concerned are the ovary, the pituitary, and the thyroid, but it is not easy always to localize the primary cause, or to tell why it should occur. In the normal amenorrhea that comes with the menopause, certainly it is in the ovary that the primary break is noted, presumably as an expression of a natural limitation of the functional life span of that organ. That primary ovarian failure may occur prematurely is indicated by the occurrence of an amenorrhea which is intractable to treatment, which is accompanied by disappearance of estrin and persistence of pituitary hormone in the urine, with at times vasomotor and other subjective menopausal symptoms. The endometrium in such cases is characteristically atrophic. Such a picture would seem to leave no doubt of the primarily hypogonadal nature of the amenorrhea, constituting what is essentially a premature and almost always a permanent menopause.

As opposed to this group, there is another in which, chiefly because of the absence of any evidence of pituitary and thyroid disorder, the clinical assumption again is that the primary cause must be hypogonadal. In many of these, however, it is probable that the ovaries are capable of function were the pituitary stimulus normal. Not all cases of pituitary amenorrhea are of the adiposogenital dystrophy type, for the adiposity and other metabolic components of the Fröhlich syndrome are not due to pituitary sex hormone disorder, but to accompanying disturbance in the parahypophyseal regions of the brain, especially the hypothalamus. While the pituitary and the parapituitary disorders are usually associated, as in Fröhlich's syndrome, either one may occur without the other. Thus it is possible to have pituitary amenorrhea in patients of perfectly normal build and weight, and with normal basal rates. On the other hand, I have seen a number of patients with all the characteristics of Fröhlich's syndrome, such as the rather abrupt development of obesity of typical so-called pituitary distribution, in whom menstruation has nevertheless continued normal in amount and periodicity. Figs. 1 and 2 illustrate such a patient, whose weight had several years previously increased rather quickly from 160 to 232 pounds. The heavy shoulder

pads, the large busts, the comparatively small waist, the heavy girdle of fat about the abdomen, buttocks, and hips, and the small hands and feet, all seem characteristic of the Fröhlich type; and yet the pituitary sex hormones are apparently functioning quite normally, as indicated by the normal menstrual function.

It is this cerebral type of obesity which is so difficult to treat with any success, and which, as I pointed out in a recent paper, is at times associated with disturbance of the water balance. In a certain group of cases, the course of the condition may be marked by remarkable weight in-



Fig. 1.

Fig. 2.

Fig. 1.—Patient, aged twenty-six years, had increased in weight rather abruptly from 160 to 222 pounds, the distribution of fat being of so-called "hypopituitary" type, but menstruation was normal in every respect.

Fig. 2.—Posterior view of patient shown in Fig. 1.

creases during menstruation, with rapid drop after the period, accompanied often by polyuria. To add to the confusion, and to illustrate further how we must try to differentiate the results of disturbances in this region on the basis not of organs but of individual centers, one may encounter menstrual edema in girls who are not obese and whose menstrual function is normal. I have seen menstrual edema, with a gain of even fifteen pounds during the periods, and with very evident swelling

of the face and extremities, in girls of perfectly normal weight and with entirely normal menstruation. Here there is a disturbance rather sharply localized in the areas and cells concerned with water and chloride balance. The fact that there is a definite menstruation-like rhythm with these extrahypophyseal cerebral disturbances is suggestive, lending support to the view, urged by Hohlweg and Junkmann² on the basis of experimental work, that behind and beyond the pituitary, as it were, there are sex centers situated in the region of the midbrain to which we must look for the explanation of many of the more fundamental characteristics of the reproductive cycle, such as its periodicity.

Such a concept, too, may help us in the explanation of such phenomena as the vasomotor symptoms of the menopause, in which both nervous and endocrine factors must be concerned. It is possibly important also in the consideration of the psychic disturbances of menstrual function and of gestation which are at times encountered. Perhaps when we know more of the nerve pathways between the sex center areas of the brain and other cerebral centers, we may be given a new understanding of segmental disturbances of fat distribution, such as those seen in lipodystrophia progressiva, in which disappearance of the subcutaneous fat in the upper part of the body and its increase in the lower part make any purely endocrine explanation almost untenable.

With reference to the relation of the thyroid to the gonads, we know comparatively little, though a relationship of some sort is indicated, not only by such clinical phenomena as menstrual swelling of the thyroid, but also by the frequency of menstrual disorders with either hypo- or hyper-function of the thyroid. The demonstration in recent years that the hypophysis, through a thyreotropic principle, dominates thyroid function, just as it does that of the ovary, has suggested to some that the thyreo-ovarian relationship may perhaps be an indirect one, mediated through the pituitary. And yet it is difficult to escape the feeling that this is not the whole story, and that the thyroid may exercise some direct influence on one or more links of the menstrual chain.

Though there is no worth-while evidence on the point, the frequent success of thyroid therapy in cases of sterility suggests that it is the germ plasm of the sex cell which may be thus affected. I have already mentioned the fact that a small proportion of normally menstruating women are sterile because they do not ovulate. There are probably a considerable number who do ovulate, but in whom the eggs are of such inferior grade that they cannot, so to speak, take the male charge. Where the germ cell inferiority is not so marked, fertilization may occur, but the resulting pregnancy "peters out" at various stages. In still others, pregnancy may continue to term, with either stillbirth or the birth of a puny infant that soon succumbs. Finally, with eggs of good quality, the initial impulse is sufficient to ensure a healthy child and normal life

expectancy. This factor of defective germ plasm as a cause of sterility and "idiopathic" miscarriage is now accepted by all embryologists (Streeter),³ and there is some reason to believe, chiefly on the basis of the frequent value of thyroid therapy in such cases, that it is this factor which is influenced by the thyroid.

In this connection I may call attention to a very recent study made by Young and Blandau⁴ upon guinea pigs. This investigation was directed to determining the relationship between the age of the ovum and the course of gestation and development. As might be expected in view of other studies, the percentage of impregnations following insemination decreases as ovum age (after ovulation) increases, the extreme limit of ovum viability being found to be twenty-six hours. Of chief interest, perhaps, was the high incidence of embryonic death noted when the older ova are fertilized. In the guinea pig, therefore, it would seem that defects in the ovum due to its age may be an important cause of miscarriage. The suggestion would be that other defects of germ plasm might likewise be responsible for abnormalities of embryonic development, and quite probably in human beings as well as in the lower animals.

There are many other aspects of ovarian dysfunction which invite discussion, and most of them have important practical bearings upon clinical problems, such as dysmenorrhea, sterility, habitual abortion, menopausal symptoms, gonorrheal vaginitis in children, etc., but it would obviously be impossible to discuss them all within the limits of a paper of considerate length. One other subject, however, I cannot refrain from touching upon, because it constitutes the most important recent development in gynecologic endocrinology. I refer to the new knowledge which has been gained concerning the chemistry of the sex hormones, the demonstration of the chemical kinship of the two ovarian hormones, one with another, and also with the male sex hormone. I shall go into no detail on this subject, especially as I have reviewed it in a recent paper.

Even more interesting, perhaps, has been the revelation that the structural formula of all these hormones is similar to that of certain well-known chemical substances of the sterol group, and that estrous phenomena can be elicited in castrated animals by the injection of these non-hormonal chemicals as well as by the estrogenic hormones themselves. A tremendous impetus has been given to the chemical study of the whole group of estrogenic substances, and many derivatives have been described, with marked differences in the degree of estrogenic potency. The possibility of synthetic preparation of estrogenic substances, as well as of progesterone, has become a very real one. Already, for example, it has been possible to synthesize progesterone from pregnyl, a substance found in the urine of pregnancy, whereas the only source hitherto has been the corpus luteum itself. This does not, of course, mean that

the synthetic process is as yet practical from a commercial standpoint, for such is not the case, but it does make it very probable that such methods are reasonably sure to come in the not very distant future.

From the standpoint of medical science in general, one of the most provocative of all the discoveries in this rich field has been that a close chemical affinity exists between the estrogenic substances and certain well-known carcinogenic substances, particularly the tar derivatives. Certain of the latter are definitely estrogenic, while a considerable amount of evidence has already been accumulated to indicate that the estrogenic substances under certain conditions may be carcinogenic. This is a long story in itself, and I have summarized it in a recent paper with Yui.⁵ In this paper we have also presented some evidence to suggest the carcinogenic tendencies of estrin upon the endometrium of women beyond the menopause.

An interesting development of recent years has been the frequent finding of estrin in the urine of women long after the menopause, and even long after surgical castration. This would seem to preclude the possibility of the ovaries as a source of the estrogenic principle. Whether estrin production may be assumed by some other endocrine organ after removal of the ovaries, as is done by the placenta during pregnancy, or whether the postmenopausal estrin is a chemical metabolite of some sort, we cannot say.

Our own study, based on the review of 864 cases of hyperplasia, showed this lesion to be not very rare in women well beyond the menopause, this observation checking with the occasional finding of estrin in the urine of elderly women, as above mentioned. Our study included a review of 104 cases of adenocarcinoma of the fundus during the same eleven-year period, with the disclosure that the noncancerous endometrium in this group showed a disproportionately high incidence of hyperplasia, even though the women were well beyond the menopause.

The inference would seem justified, therefore, that a postmenopausal endometrium subjected to persistent estrogenic stimulation is predisposed to adenocarcinoma. This observation is in accordance with Loeb's conclusion, after a thorough review of the problem, that estrogenic substances have been demonstrated to be carcinogenic in those tissues and organs which are normally under the physiologic control of estrin. This would apply especially to the uterus and the breast. In the latter organ the long-continued injection of estrin has apparently produced cancer in a surprising proportion of cases, and the malignant process thus initiated has run its usual course even after the hormone has been withdrawn. Cancerlike pictures have been produced in the same way in the cervix, although, so far as I know, none of these lesions has continued after hormone administration has been stopped.

Such observations have opened up an entirely new lead in cancer investigation, and one which is sure to yield interesting results regardless

of whether or not they bring us closer to the solution of cancer etiology. This new application of endocrinology to the problems of human disease is but another of the many developments which justify the early hopes and enthusiasm of those who were farsighted enough to interest themselves in the subject in its earlier days, when the ductless gland enthusiast, however honest and earnest, was looked upon with condescension, if not derision, because of the motley crew of pseudoscientific ragamuffins and commercialists who crowded under the same banner. Within the short period of a quarter of a century, the tone of endocrinology has been immeasurably elevated, in spite of rapid advances which would almost excuse immoderate enthusiasm. No more brilliant chapter has been added to the scroll of medical science than that contributed by endocrinologists, and yet the wisest and most conservative among them all agree that only the surface has as yet been scratched, and that what has already been accomplished merely foreshadows even richer possibilities in the future. Small wonder, therefore, that anatomists, physiologists, and chemists have manifested such widespread interest in endocrine research, and that more and more clinicians, especially the younger men of our profession, have come to appreciate the indispensability of endocrinology in the everyday interpretation of clinical problems.

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Gray, Laman A.: **Lymphogranuloma Inguinale of the Female Urethra**, Surg. Gynec. Obst. 62: 745, 1936.

Eleven cases of this disease affecting the female urethra are reported. The disease presents a syndrome consisting of: a chronic urethritis, with or without intraurethral ulceration, which may remain extremely chronic and indolent or may proceed to urethral stricture, or to ulcerative destruction of the urethra; an ulceration which may extend beneath the clitoris and labia, or around the introitus and deeply to the sides of the rectum; and possibly an associated elephantiasis vulvae.

The presence of positive Frei reactions in 9 of the 11 cases indicates that this syndrome is probably due to the virus of lymphopathia venereum, "lymphogranuloma inguinale."

A wide variety of parenteral and local treatments had no appreciable influence on the disease. Two patients with least treatment showed the greatest healing. The indications are that cure, as in other virus diseases, probably depends on immunity.

WM. C. HENSKE.

THE ETIOLOGY AND TREATMENT OF PRIMARY DYSMENORRHEA*

A PHYSIOLOGIC AND CLINICAL STUDY

JULIUS E. LACKNER, M.D., LEON KROHN, M.D., AND
SAMUEL SOSKIN, M.D., CHICAGO, ILL.

*(From the Department of Gynecology and Obstetrics and the Department of
Metabolism and Endocrinology of Michael Reese Hospital)*

THE multiplicity of factors involved in dysmenorrhea has given rise to many conflicting theories as regards its etiology, none of which have supplied a completely adequate explanation. It is not our purpose, at the present time, to review in detail the ideas advanced by Novak and Reynolds,¹ Kennedy,² Israel,³ and others. Suffice it to say that the recent advances in the field of endocrinology have directed attention to the endocrine aspects of dysmenorrhea and it is from this point of view that primary or functional dysmenorrhea is now generally regarded.

It is well established that the estrogenic substances augment, and that progesterone decreases the motility of the uterus, in various laboratory animals. Similar observations have been made by Falls, Lackner and Krohn⁴ on the puerperal human uterus. The present authors have recently demonstrated that the same applies to the normal nonpregnant and nonpuerperal human uterus.⁵ In view of these facts it would seem logical to conclude, as Novak and Reynolds¹ have done, that the pain in primary dysmenorrhea is due to an exaggerated contractility of the uterus, consequent to a faulty balance of the above hormones at the menstrual period. Moir,⁶ who recorded the uterine contractions in a patient suffering from severe dysmenorrhea, carried the analogy between uterine pain and pain in other muscular organs, a step farther. He observed that the sensation of greatest discomfort coincided with the peak of each contraction, and that each peak was marked by a disappearance of the arterial pulsation, which was superimposed on the other portions of his graphic record. He, therefore, suggested that the pain in dysmenorrhea might be associated with a relative ischemia of the uterus, as has been supposed to occur in the heart with angina pectoris, and in the skeletal muscle with intermittent claudication.

Another endocrine theory of dysmenorrhea has been advanced by Kennedy,² who believes that it is associated with degenerative changes in Frankenhauser's ganglion, as a result of a deficiency of estrin. Aside

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TABLE I. SUMMARY OF RESULTS

CASE	DIAGNOSIS	FIRST DAY OF MENSES BEFORE TREATMENT						FIRST DAY OF MENSES AFTER TREATMENT								
		UTERINE CONTRAC- TIONS	UTERINE ENDO- METRIUM	URINE ESTRIN			BLOOD	TREATMENT	PAIN	UTERINE CONTRAC- TIONS	UTERINE ENDOMETRIUM	URINE ESTRIN		BLOOD		
				FREE	COMBINED	ESTRIN						PROLAN	FREE		COMBINED	ESTRIN
C. L.	Normal	Very large	Cervical epithelium and glands	30	120	-	+	0	0							
M. G.	Normal	Moderate	Secretory	30	30	-	-	0	0							
H. W.	Normal	Large	Hyper- plastic	30	30	-	-	0	0							
P. G.	Normal	Large	Prolifera- tive	120	120	+	-	0	0							
E. R.	Primary dysmenorrhea	Large	Prolifera- tive	180	180	+	-	Progesterone	Relieved	Moderate	Secretory	<30	30	-		-
M. Gu.	Primary dysmenorrhea	Very large	Early secretory			+	-	Progesterone	Relieved	Very large	Early secretory			-		-
E. S.	Primary dysmenorrhea	Large	Atrophic	<30	30	-	-	Progesterone	Relieved	Large	Proliferative	<30	30	-		-
M. W.	Primary dysmenorrhea	Very large	Secretory	<30	30	-	-	Progesterone	Relieved	Moderate	Secretory	<30	<30	+		-
G. L.	Primary dysmenorrhea	Large	Secretory	<30	<30	-	-	Progesterone	Relieved	Moderate	Early secretory	<30	30	-		-
K. W.	Primary dysmenorrhea	Large	Secretory	<30	<30	-	-	Estrogenic substance	Relieved	Moderate	Hyperplastic	30	30	-		-
N. M.	Primary dysmenorrhea	None	Insufficient	60	60	-	-	Estrogenic substance	Relieved	Small	Late proliferative	120	180	+		-
P. Gi.	Primary dysmenorrhea	Small	Prolifera- tive	30	60	-	+	Estrogenic substance	Relieved	Moderate	Insufficient	30	60	-		+
G. N.	Primary dysmenorrhea	Large	Hyper- plastic	30	60	-	-	Progesterone	No relief	Large	Late proliferative	120	120	+		-
E. A.	Primary dysmenorrhea	Large tetanic	Hyper- plastic	120	120	-	-	Progesterone	No relief	Large	Proliferative	<30	<30	-		-
E. A.	Primary dysmenorrhea	Large tetanic	Hyper- plastic	120	120	-	-	Estrogenic substance	Slight relief	Large	Proliferative	<30	30	-		-

from the opposing theoretical considerations involved in this and the theory outlined above, the two hypotheses present a practical conflict in therapeutics. If one is to act on the belief that dysmenorrhea is caused

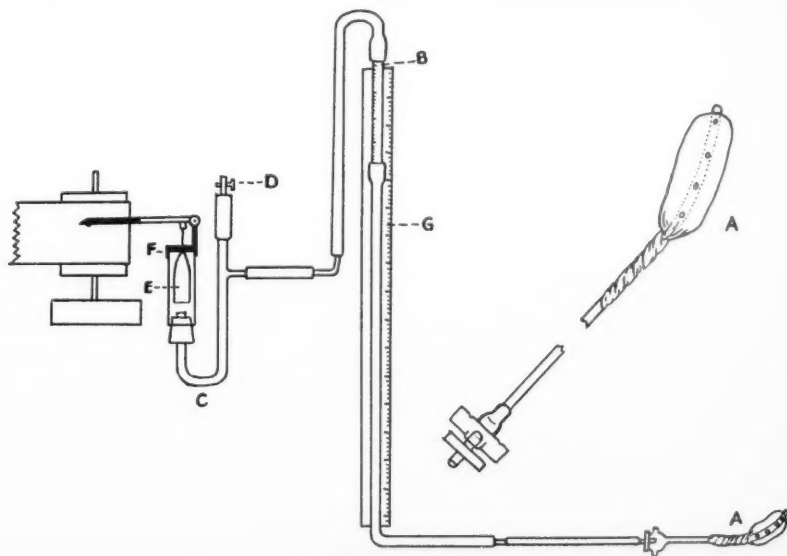


Fig. 1.—Apparatus for recording uterine motility at known volume and pressure. (A) Balloon ensemble, (B) calibrated leveling tube, (C) water manometer, (D) stopcock, (E) Balsa-wood float, (F) metal cap supporting the recording lever, and (G) movable scale.

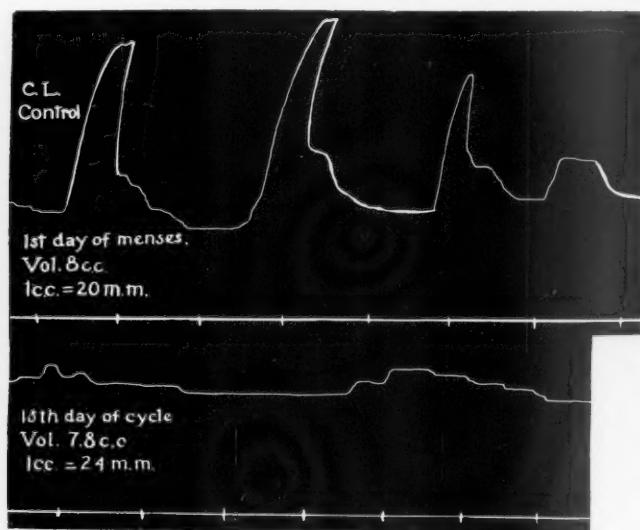


Fig. 2.—Uterine motility in a normal control on the first and fifteenth days of the menstrual cycle. Photographic reduction $4\frac{1}{2}$ times.

by an exaggerated contractility of the uterus due to a relative preponderance of estrin, the logical treatment is the administration of progester-

TABLE II. CASE C. L., AGED TWENTY-ONE YEARS, PARA II. CONTROL

	MIDPERIOD	FIRST DAY OF MENSES
Volume of uterus	7.8 c.c.	8.0 c.c.
Contractions	Small, irregular	Very large, regular 1 every 2 minutes
Blood	Prolan, minus Estrin, minus	Prolan, plus Estrin, minus
Urine estrin	Free < 30 Combined < 30	Free 30 Combined 120
Endometrium	Proliferating	Cervical epithelium and glands

one, as applied by Campbell and Hisaw,⁷ and Elden and Wilson.⁸ Or, an increase in available progesterone in the individual may be secondarily induced by the administration of the luteinizing principle of pregnancy urine, as advocated by Novak and Reynolds,¹ Browne,⁹ and

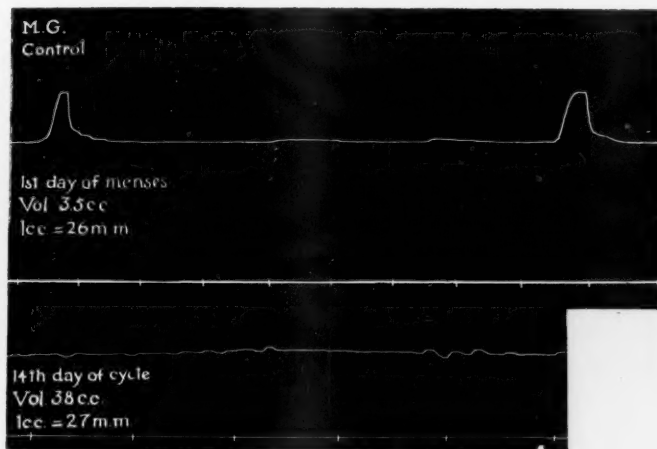


Fig. 3.—Uterine motility in a normal control on the first and fourteenth days of the menstrual cycle. Photographic reduction $3\frac{1}{2}$ times.

TABLE III. CASE M. G., AGED TWENTY-THREE, PARA I. CONTROL

	MIDPERIOD	FIRST DAY OF MENSES
Volume of uterus	3.8 c.c.	3.5 c.c.
Contractions	Small, irregular	Moderate, regular 1 every five minutes
Blood	Prolan, minus Estrin, minus	Prolan, minus Estrin, minus
Urine estrin	Free < 30 Combined 60	Free 30 Combined 30
Endometrium	Proliferating	Secretory

Witherspoon.¹⁰ According to this view the administration of estrogenic substance would actually aggravate the dysmenorrhea. Whereas, if one accepts the views of Kennedy, estrogenic substance is the treatment of choice.

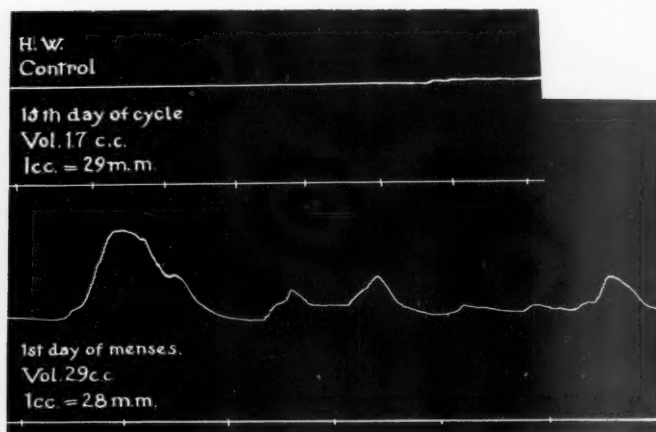


Fig. 4.—Uterine motility in a normal control on the first and fifteenth days of the menstrual cycle. Photographic reduction 3 times.

TABLE IV. CASE H. W., AGED THIRTY-NINE, PARA 0. CONTROL

	MIDPERIOD	FIRST DAY OF MENSES
Volume of uterus	1.7 c.c.	2.9 c.c.
Contractions	None	Large, fairly regular About 1 per minute
Blood	Prolan, minus Estrin, minus	Prolan, minus Estrin, minus
Urine estrin	Free 30 Combined 30	Free 30 Combined 30
Endometrium	Insufficient	Hyperplastic

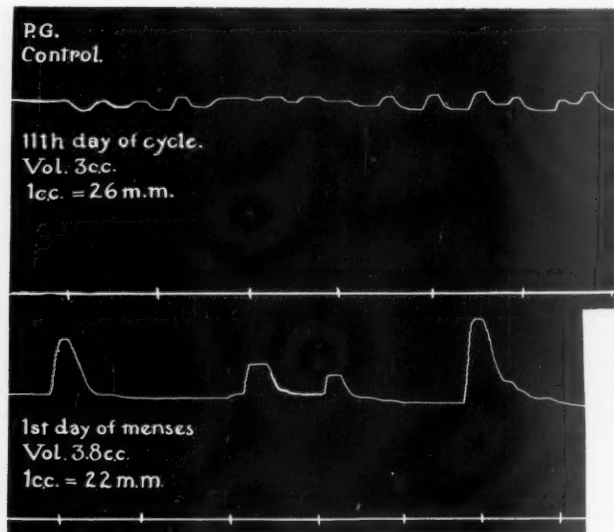


Fig. 5.—Uterine motility in a normal control on the first and eleventh days of the menstrual cycle. Photographic reduction $3\frac{1}{2}$ times.

TABLE V. CASE P. G., AGED THIRTY-FIVE, PARA II. CONTROL

	MIDPERIOD	FIRST DAY OF MENSES
Volume of uterus	3.0 c.c.	3.8 c.c.
Contractions	Small, fairly regular 2 per minute	Large, fairly regular 1 every 2 minutes
Blood	Prolan, minus Estrin, plus	Prolan, minus Estrin, plus
Urine estrin	Free 60 Combined 120	Free 120 Combined 120
Endometrium	Proliferative	Proliferative

It appeared to us likely that the two mechanisms described in the above hypotheses were not mutually exclusive, but that each of them, and perhaps other factors, operated in different groups of patients. It there-

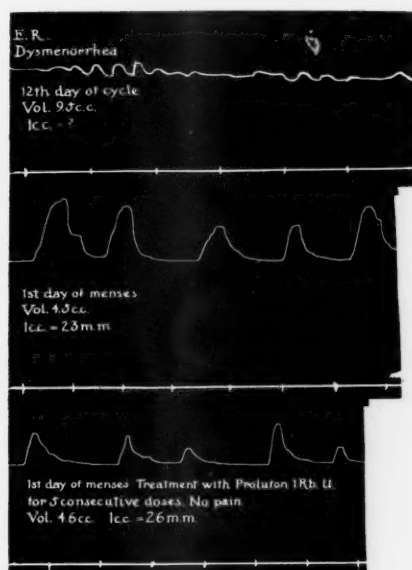


Fig. 6.—Uterine motility in a patient with dysmenorrhea on the first and twelfth days of the menstrual cycle before treatment, and on the first day of menstruation after treatment with progesterone. Photographic reduction 3 times.

TABLE VI. CASE E. R., AGED TWENTY-ONE, PARA I. DYSMENORRHEA

	MIDPERIOD	FIRST DAY OF MENSES	FIRST DAY OF MENSES SUBSEQUENT TO TREATMENT WITH PROGESTERONE
Pain	None	Severe	None
Volume of uterus	9.5 c.c.	4.5 c.c.	4.6 c.c.
Contractions	Small, 2-3 per minute	Large, 1-1½ minutes apart	Moderate 1-1½ minutes apart
Blood	Prolan, minus Estrin, plus	Prolan, minus Estrin, plus	Prolan, minus Estrin, minus
Urine estrin	Free 120 I.U. Combined 120 I.U.	Free 180 I.U. Combined 180 I.U.	Free < 30 I.U. Combined 30 I.U.
Endometrium	Insufficient	Proliferative	Secretory

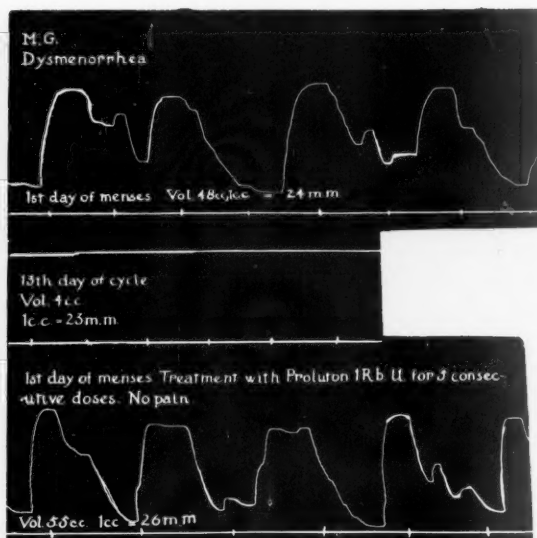


Fig. 7.—Uterine motility in a patient with dysmenorrhea on the first and thirteenth days of the menstrual cycle before treatment, and on the first day of menstruation after treatment with progesterone. Photographic reduction 4 times.

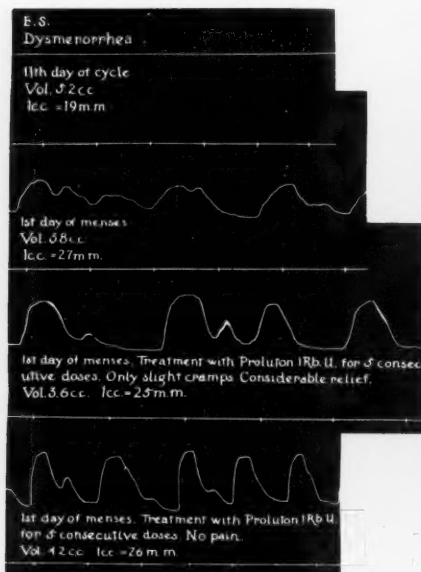


Fig. 8.

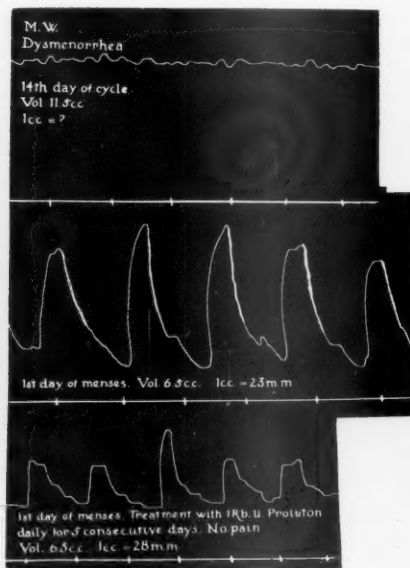


Fig. 9.

Fig. 8.—Uterine motility in a patient with dysmenorrhea on the first and eleventh days of the menstrual cycle before treatment, and on the first day of menstruation after treatment with progesterone. Photographic reduction 4 times.

Fig. 9.—Uterine motility in a patient with dysmenorrhea on the first and fourteenth days of the menstrual cycle before treatment, and on the first day of menstruation after treatment with progesterone. Photographic reduction 5 times.

fore seemed important to study a number of women suffering from primary dysmenorrhea with a view to differentiating the various types of

TABLE VII. CASE M. Gu., AGED TWENTY-ONE, PARA I. DYSMENORRHEA

	MIDPERIOD	FIRST DAY OF MENSES	FIRST DAY OF MENSES SUBSEQUENT TO TREATMENT WITH PROGESTERONE
Pain	None	Severe	None
Volume of uterus	4 c.c.	4.8 c.c.	5.5 c.c.
Contractions	None	Very large. Regular. 1 every 2 minutes	Very large, regular 1 every minute
Blood	Prolan, minus Estrin, minus	Prolan, minus Estrin, plus	Prolan, minus Estrin, minus
Urine estrin	Free < 30 Combined < 30		
Endometrium	Late proliferative	Early secretory	Early secretory

TABLE VIII. CASE E. S., AGED TWENTY-FOUR, PARA 0. DYSMENORRHEA

	MIDPERIOD	FIRST DAY OF MENSES	FIRST DAY OF MENSES SUBSEQUENT TO TREATMENT WITH PROGESTERONE
Pain	None	Very severe	Slight discomfort
Volume of uterus	5.2 c.c.	3.8 c.c.	4.2 c.c.
Contractions	None	Large, regular 1 per minute	Large, regular 1 per minute
Blood	Prolan, plus Estrin, plus	Prolan, minus Estrin, minus	Prolan, minus Estrin, minus
Urine estrin	Free 60 Combined 60	Free < 30 Combined 30	Free < 30 Combined 30
Endometrium	Proliferative	Atrophic	Proliferative

TABLE IX. CASE M. W., AGED TWENTY-SIX, PARA I. DYSMENORRHEA

	MIDPERIOD	FIRST DAY OF MENSES	FIRST DAY OF MENSES SUBSEQUENT TO TREATMENT WITH PROGESTERONE
Pain	None	Moderately severe	None
Volume of uterus	11.5 c.c.	6.5 c.c.	6.3 c.c.
Contractions	Irregular, small 3 per minute	Very large, regular 1 per minute	Moderate, regular 1 per minute
Blood	Prolan, minus Estrin, minus	Prolan, minus Estrin, minus	Prolan, minus Estrin, plus
Urine estrin	Free 45 Combined 45	Free < 30 Combined 30	Free < 30 Combined < 30
Endometrium	Proliferative	Secretory	Secretory

cases, and with the hope of establishing criteria by which they might be distinguished from each other.

PROCEDURE

The nature of the methods which we employed precluded the possibility of a statistical study on a large number of patients. Instead, a small group of women suffering from primary dysmenorrhea and a few normal women were studied as intensively and as objectively as possible. Graphic records of uterine motility, biopsies of the uterine endometrium, and hormone assays of the blood and urine were made simultaneously in each subject, at certain intervals. In four normal women these observations were made at the midperiod and on the first day of menstruation. In ten dysmenorrheic women these observations were made at the midperiod, on the first day of menstruation when pain was present, and on the first day of a subsequent menstrual period or periods after the patient had received endocrine therapy.

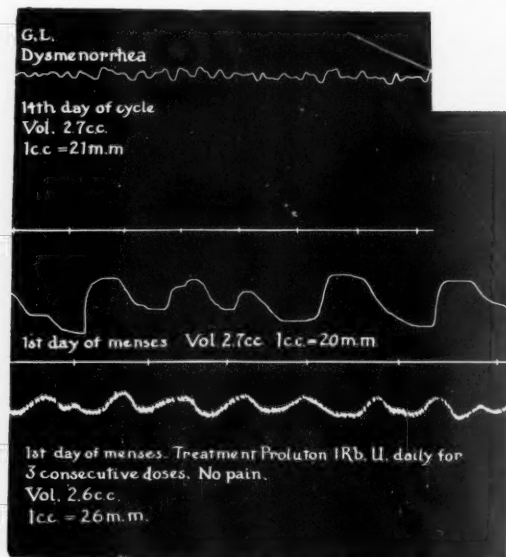


Fig. 10.—Uterine motility in a patient with dysmenorrhea on the first and fourteenth days of the menstrual cycle before treatment, and on the first day of menstruation after treatment with progesterone. Photographic reduction 4 times.

TABLE X. CASE G. L., AGED THIRTY, PARA 0. DYSMENORRHEA

	MIDPERIOD	FIRST DAY OF MENSES	FIRST DAY OF MENSES SUBSEQUENT TO TREATMENT WITH PROGESTERONE
Pain	None	Moderately severe	None
Volume of uterus	2.7 c.c.	2.7 c.c.	2.6 c.c.
Contractions	Small, fairly regular, 2-3 per minute	Large, fairly regular, 1 per minute	Moderate, regular 2 per minute
Blood	Prolan, minus Estrin, minus	Prolan, minus Estrin, minus	Prolan, minus Estrin, minus
Urine estrin	Free < 30 Combined 30	Free < 30 Combined < 30	Free < 30 Combined 30
Endometrium	Early secretory	Secretory	Early secretory

The methods used for the above purposes have been described in detail in another communication.⁵ Briefly summarized they are as follows:

Uterine motility was recorded, at a known intrauterine pressure and volume, by means of a rubber balloon inserted into the uterus, and connected through a calibrated leveling device to a new type of recording water manometer (Fig. 1). In connection with the use of the sterilized rubber balloon in the uterus it may be of interest to note that, in approximately eighty tests, we have experienced practically no difficulty as regards its insertion or withdrawal. Preliminary dilatation of the cervix has never been necessary. The one case of relative stenosis of the cervix which we encountered was in an apparently normal woman, who did not complain of dysmenorrhea. The presence of the balloon in the uterus occasionally caused slight discomfort, but in no instance have we observed after-effects of any kind.

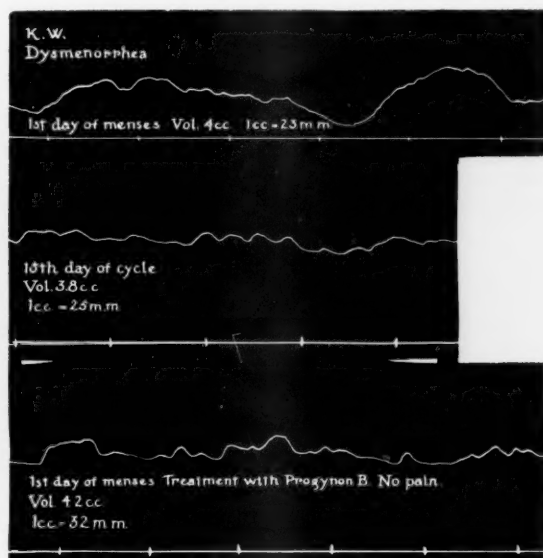


Fig. 11.—Uterine motility in a patient with dysmenorrhea on the first and fifteenth days of the menstrual cycle before treatment, and on the first day of menstruation after treatment with estrogenic substance. Photographic reduction 4 times.

TABLE XI. CASE K. W., AGED THIRTY-FOUR, PARA 0. DYSMENORRHEA

	MIDPERIOD	FIRST DAY OF MENSES	FIRST DAY OF MENSES SUBSEQUENT TO TREATMENT WITH ESTROGENIC SUBSTANCE
Pain	None	Severe	None
Volume of uterus	3.8 c.c.	4 c.c.	4.2 c.c.
Contractions	Small, fairly regular. 3 per minute	Large, irregular occasionally tetanic	Moderate, irregular 2 per minute
Blood	Prolan, plus Estrin, plus	Prolan, minus Estrin, minus	Prolan, minus Estrin, minus
Urine estrin	Free 30 Combined 240	Free < 30 Combined < 30	Free 30 Combined 30
Endometrium	Secretory	Secretory	Hyperplastic

Endometrial biopsies were obtained with Novak's suction curette.¹¹ To make sure of getting a true picture of the entire endometrium, we took several strips from different parts of the uterus (Figs. 16 to 19).

The acetone precipitation¹² and tungstic acid precipitation¹³ methods respectively, both previously reported from this laboratory, were used to assay the estrogenic and gonadotropic hormones in the blood samples, and the free and total estrin in the twenty-four-hour urine specimens. The gonadotropic hormone in the urine was not estimated since it is known to parallel that in the blood.¹⁴ In the assay of blood estrin the test was called positive when the extract from 40 c.c. of blood produced a cornified smear in a castrated mouse in forty-eight to sixty hours, signifying at least 25 mouse units per liter. The test for gonadotropic hormone in the blood was considered positive when the extract from 40 c.c. of blood produced an Aschheim-Zondek reaction in twenty-three- to twenty-five-day-old rats, in one hundred hours.

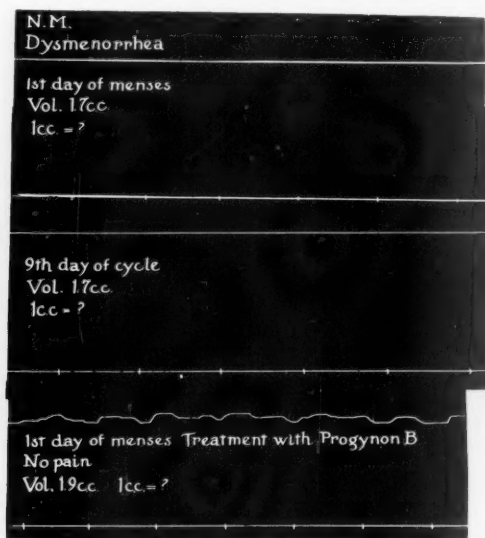


Fig. 12.—Uterine motility in a patient with dysmenorrhea on the first and ninth days of the menstrual cycle before treatment and on the first day of menstruation after treatment with estrogenic substance. Photographic reduction $3\frac{1}{2}$ times.

TABLE XII. CASE N. M., AGED TWENTY-NINE, PARA 0. DYSMENORRHEA

	MIDPERIOD	FIRST DAY OF MENSES	FIRST DAY OF MENSES SUBSEQUENT TO TREATMENT WITH ESTROGENIC SUBSTANCE
Pain	None	Severe	None
Volume of uterus	1.7 c.c.	1.7 c.c.	1.8 c.c.
Contractions	None	None	Small, irregular 1-2 per minute
Blood		Prolan, minus Estrin, minus	Prolan, minus Estrin, plus-plus
Urine estrin		Free 60 Combined 60	Free 120 Combined 180
Endometrium	Insufficient	Insufficient	Late proliferative

The urine estrin figures, for purposes of record, have been converted from mouse units into international units which are given in our tables. In our laboratory 1 mouse unit equals 3 international units.

RESULTS

The results in each experimental subject are briefly noted in an individual tabulation (Tables II to XV) accompanied by a corresponding set of illustrative records of uterine motility (Figs. 2 to 15). Much of the data in these tables we have found difficult of correlation and interpretation, at the present state of our knowledge. These have been included for future reference and in the hope that others, from a different viewpoint, may perhaps be able to read more into them than we have. Such data, from all the above tables, as have seemed to us to have immediate significance in the interpretation of our results, have been summarized in Table I for purposes of comparison.

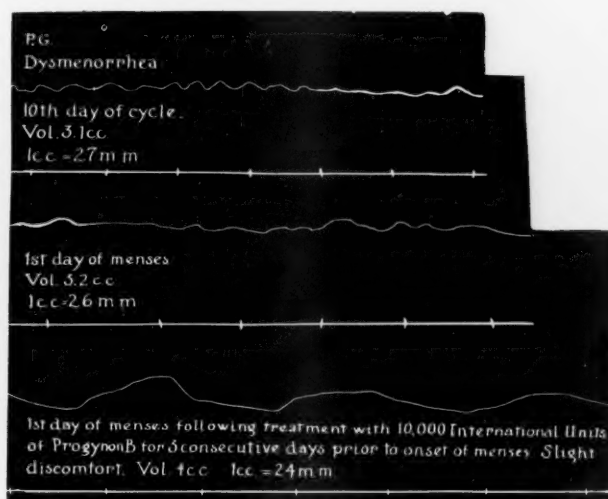


Fig. 13.—Uterine motility in a patient with dysmenorrhea on the first and tenth days of the menstrual cycle and on the first day of menstruation after treatment with estrogenic substance. Photographic reduction $3\frac{1}{2}$ times.

TABLE XIII. CASE P. G., AGED TWENTY-EIGHT, PARA 0. DYSMENORRHEA

	MIDPERIOD	FIRST DAY OF MENSES	FIRST DAY OF MENSES SUBSEQUENT TO TREATMENT WITH ESTROGENIC SUBSTANCE
Pain	None	Severe	None
Volume of uterus	3.1 c.c.	3.2 c.c.	4 c.c.
Contractions	Small, fairly regular, 3 per minute	Small, irregular spasms 2 per minute	Moderate, prolonged regular 1 every 2 minutes
Blood	Prolan, minus Estrin, minus	Prolan, plus Estrin, minus	Prolan, plus Estrin, minus
Urine estrin	Free < 30 Combined < 30	Free 30 Combined 60	Free 30 Combined 60
Endometrium	Insufficient	Proliferative	Insufficient

In all the motility records which are presented the recording pressure was 100 cm. of water, and the time markings on the base-line represent one-minute intervals.

DISCUSSION

We should like to forestall any misapprehension by being the first to disclaim that we have solved the etiology and treatment of primary dysmenorrhea. However, the least equivocal and perhaps the most practically important of our results, is the fact that we have been able to give complete relief to eight out of the ten dysmenorrheic women whom we attempted to treat with endocrine preparations. It need hardly be pointed out that these gratifying therapeutic results cannot be called "cures," since the treatment is substitutional rather than curative in

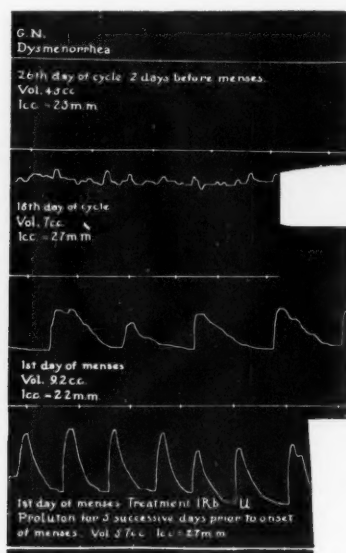


Fig. 14.—Uterine motility in a patient with dysmenorrhea on the first, fifteenth and twenty-sixth days of the menstrual cycle before treatment, and on the first day of menstruation after treatment with progesterone. Photographic reduction 6 times.

TABLE XIV. CASE G. N., AGED THIRTY-ONE, PARA III. DYSMENORRHEA

	MIDPERIOD	FIRST DAY OF MENSES	FIRST DAY OF MENSES SUBSEQUENT TO TREATMENT WITH PROGESTERONE
Pain	None	Severe	Severe
Volume of uterus	7 c.c.	9.2 c.c.	5.7 c.c.
Contractions	Small, irregular 2 per minute	Large, regular 1 per minute	Large, regular 1 per minute
Blood	Prolan, plus Estrin, plus	Prolan, minus Estrin, minus	Prolan, minus Estrin, plus
Urine estrin	Free 60 Combined 120	Free 30 Combined 60	Free 120 Combined 120
Endometrium	Secretory	Hyperplastic	Late proliferative
Therapy with estrogenic substance at a subsequent period gave slight relief.			

nature. Nevertheless, these results confirm the view that primary dysmenorrhea is largely of endocrine origin, and have at least enabled us to draw some negative conclusions as to the mechanism of the pain in dysmenorrhea, as outlined below.

On the basis of our results, the 10 patients whom we treated may be divided into 3 groups. Five were completely relieved by progesterone, 3 by estrogenic substance, while 2 patients obtained little or no relief

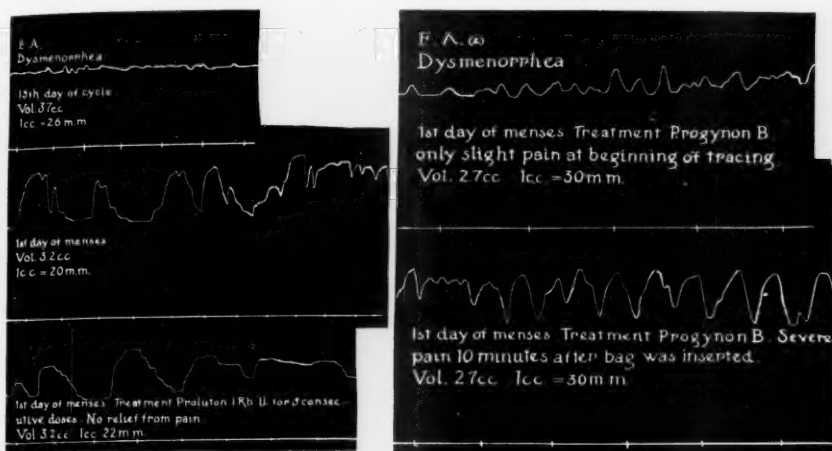


Fig. 15.—A, Uterine motility in a patient with dysmenorrhea on the first and fifteenth days of the menstrual cycle before treatment and on the first day of menstruation after treatment with progesterone. Photographic reduction 4 times. B, Uterine motility in the same patient on the first day of menstruation after treatment with estrogenic substance. Photographic reduction 3 times.

TABLE XV. CASE E. A., AGED TWENTY-FIVE, PARA 0. DYSMENORRHEA

	MIDPERIOD	FIRST DAY OF MENSES	FIRST DAY OF MENSES SUBSE- QUENT TO TREATMENT WITH PROGESTERONE	FIRST DAY OF MENSES SUBSE- QUENT TO TREAT- MENT WITH ESTROGENIC SUBSTANCE
Pain	None	Very severe	Severe	Moderate
Volume of uterus	3.7 c.c.	3.2 c.c.	3.2 c.c.	2.7 c.c.
Contractions	Small irregular	Large tetanic irregular	Large, fairly regular, 1 every 2 minutes	Small, fairly regu- lar, about 3 per minute at first. After 10 minutes large, regular, 2 per minute
Blood	Prolan, minus Estrin, minus	Prolan, minus Estrin, minus	Prolan, minus Estrin, minus	Prolan, minus Estrin, minus
Urine estrin	Free 45 Combined 180	Free 120 Combined 120	Free 30 Combined 30	Free < 30 Combined 30
Endome- trium	Slight atrophy	Early pro- liferative	Proliferative	Proliferative

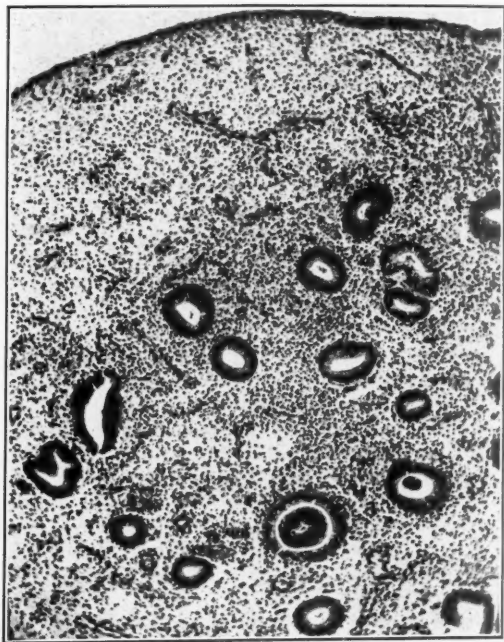


Fig. 16.—Early proliferative endometrium ($\times 75$). The thickness of the endometrium is 1.1 mm. The glands are few and straight. The epithelium is of low columnar type. The nuclei are centrally located. The stroma is loose.



Fig. 17.—Late proliferative endometrium ($\times 75$). The thickness of the endometrium is approximately 2 mm. The glands are increased in number with beginning convolution. The epithelium is unchanged.



Fig. 18.—Early secretory endometrium ($\times 75$). The thickness of the endometrium is 3 to 3.5 mm. The glands are the same in number but are now moderately convoluted. The epithelium is of tall columnar type and the nuclei are located at the base.



Fig. 19.—Late secretory endometrium ($\times 75$). The thickness of the endometrium is approximately 4 mm. The glands are typically corkscrew, dilated, and filled with secretion. The epithelial borders are frayed. The cells are packed with vacuoles. The stroma is condensed.

from either form of therapy. This distribution of results apparently confirms our prediction as to the validity, in different groups of patients, of both the hypotheses mentioned in our introductory remarks. In addition to these two types of dysmenorrhea, however, there is apparently a third type in which the mechanism is not restored to normal by either of the endocrine preparations which we used.

In none of the above groups of cases were we able to correlate strictly any of our experimental observations with the occurrence of pain, although certain tendencies were obvious. Thus, in most of the patients, large uterine contractions were recorded at the time during which pain was experienced. Furthermore, the greatest intensity of the pain usually coincided with the peak of each contraction. Nevertheless, similarly large uterine contractions were observed in normal women who never complained of dysmenorrhea; and, what is perhaps of greater significance, at least two of the women treated with progesterone showed no diminution in the size of their uterine contractions at the time that their pain was completely relieved. It is true that the other three cases treated with progesterone exhibited a decrease in the size of their uterine motility coincident with the disappearance of pain. The difference between these and the above cases may depend on the dose of the hormone which they received relative to their needs. But, at any rate, it is apparent that symptomatic relief can be produced by doses of progesterone which are less than the amount necessary to cause a demonstrable decrease in the uterine contractions. In the face of these results it would be difficult to maintain that the pain in dysmenorrhea is directly related to the intensity of the uterine contraction, even if one were to invoke the variations in the "pain threshold" as suggested by Novak and Reynolds.¹ As regards the suggestion of Moir,⁶ that the pain is related to ischemia of the uterine muscle, we have been unable to confirm his observation upon which this idea was based. In some of our cases, the arterial pulsation superimposed on the motility record persisted throughout the peaks of the contractions.

Our other experimental data showed even less direct correlation with the uterine pain than did the size of the uterine contractions. This applies alike to the frequency of the uterine contractions, to the state of the uterine endometrium, and to the titer of the hormones in the blood and urine. This is not to say that the endometrium and the hormone assays did not correspond in some cases with the grouping of the case as regards the presence of a relative preponderance of progesterone or of estrogenic substance. The difficulty rests on the fact that the same endometrial and hormonal findings were also present in certain cases which fell into opposing groups as far as the response to therapy was concerned.

It is clear that our efforts to discover the actual cause of the pain in dysmenorrhea must be extended to other channels and methods. Our

results, fruitless in this regard, have nevertheless yielded information of some practical importance. Thus the dysmenorrheic patient with a large, well-developed uterus which exhibits moderate to large contractions, usually obtains complete relief from pain after treatment with progesterone. The patient with the small hypoplastic uterus, which shows little or no contraction, is likely to respond favorably to estrogenic substance. Using these simple criteria for the proper selection of cases, it should be possible completely to relieve a large proportion of the women who regularly suffer from this common and disabling form of pain.

CONCLUSIONS

1. Eight out of ten women, suffering from primary dysmenorrhea, have been completely, though temporarily, relieved by endocrine therapy. This form of dysmenorrhea may therefore be regarded as being largely of endocrine origin.

2. The patients whom we studied and treated may be divided into three groups: Those who were relieved by progesterone, those who responded to estrogenic substance, and those in whom neither of these substances was effective.

3. We have been unable to establish any strict correlation between the occurrence of menstrual pain and of uterine contractions, the state of the uterine endometrium, or the hormone content of blood and urine.

4. Certain simple and general criteria have been outlined to aid in the proper selection of cases for treatment with progesterone and estrogenic substance respectively.

NOTE.—We are indebted to Dr. Gregory Stragnell of the Schering Corporation for ample supplies of progynon B and proluton; to Dr. Otto Saphir for generous cooperation with the histologic interpretations; and to Dr. S. Charles Freed for the performance of the arduous task of assaying many samples of blood and urine for their hormone content.

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DISCUSSION

DR. JEAN PAUL PRATT, DETROIT, MICH.—The chief value of the contribution is found in the attempt to establish a causal relation for hormonal therapy. Yet the authors have wavered a little in their interpretation. In evidence of this is their third conclusion: "We have been unable to establish any strict correlation between the occurrence of menstrual pain and of uterine contractions, the state of uterine endometrium, or the hormone content of the blood and urine." They answer their own question about the fallibility of endocrine therapy.

Regarding the experiments we should know how long a foreign body can be retained in the uterus without causing irritation. Most of the curves represent only four contractions extending over a few minutes. It is important to know what a longer curve would show. In the first control, for example, the first contraction is very high, the second high, the third low, and the fourth not quite so low. Therefore even in four consecutive contractions, there is a wide variation. It is very difficult, as they have stated already, to correlate the different curves. Finally, the curves presented are too few to permit conclusions. I should like to have these authors continue with their work and present a list of 100 controls.

DR. KROHN (closing).—It is true that only a small number of controls are included in this report. This was because of the extreme difficulty encountered in securing normal women willing to lend themselves to this type of study.

The slides we demonstrated were photographs of a typical section of the original tracings of the uterine motility. The kymographic records were very long, since we usually allowed the intrauterine bag to remain in place for from two to three hours. The contractions on each individual record did not vary a great deal. In the normal control cases, the volume of the uterus seemed to be in direct proportion with the size of the uterine contractions. That is, large contractions were recorded from patients with a large uterine volume and when the uterine volume was small, the contractions were correspondingly small.

Lepontre, C.: *Pyelitis of Defloration*, Bull. Soc. d'obst. et de gynec. 25: 701, 1936.

The author reports his experience with pyelitis which follows defloration. The pyelitis in these cases has been attributed to infection which results from rupture of the hymen and also to trauma at the urethral orifice during attempts at coitus in women who have a high perineum and a narrow vaginal introitus. These cases are often erroneously attributed to a gonorrheal infection transmitted by the husband. The consequences of such an error may be very serious. The mistake may be avoided by examining the urine microscopically, for only colon bacilli will be found.

In the discussion of this paper Delannoy took exception to the name pyelitis of defloration. He attributes this pyelitis to a change in the manner of living of young married people and the fatigue of a honeymoon, and hence he thinks a better term is pyelitis of the honeymoon.

J. P. GREENHILL.

Ch'in, T. L., and Lim, K. T.: *The Yeast-Like Fungi Found in the Vagina of Pregnant and Non-Pregnant Women*, Chinese M. J. 50: 1211, 1936.

The authors made 200 vaginal cultures, 100 from pregnant and 100 from non-pregnant women. Among the pregnant cases there were 39 patients positive for yeasts, while in the nonpregnant cases there were 11. In the pregnant cases the yeasts were more frequently found in young women, and also in the latter part of pregnancy. This difference is most probably due to a higher glycogen content in the vaginal mucosa of pregnant women, a condition favoring the growth of yeasts and promoting the formation of an acid medium unfavorable to most bacterial organisms.

C. O. MALAND.

A STUDY OF FIVE PATIENTS WITH CHORIONEPITHELIOMA*

JAMES A. GOUGH, M.D., CHICAGO, ILL.

(From the Department of Obstetrics and Gynecology, St. Luke's Hospital)

CHORIONEPITHELIOMA when originally described by Saenger in 1889 was considered decidual in origin and designated "sarcoma uteri deciduocellulare." By 1895 several other reports had been published, among them those by Williams and Marchand. The latter correctly ascribed the origin of the cellular elements to the fetal trophoblast and introduced the name now in use. During the next thirty years many isolated case reports were published. Much of this is difficult to evaluate because, as a rule, only in rare instances did the author observe more than one case. The novelty of the diagnosis also may have resulted in publications not entirely acceptable to more critical readers.

The pitfalls in histologic diagnosis were recognized by most observers, but no test was available which would substantiate or refute the impression aroused by the microscope. In 1928 Aschheim and Zondek, on the basis of hormone studies, offered a test for determining pregnancy which has enhanced the methods for detecting the presence of chorionepithelioma. Today the histologic structure of tissues is supplemented by this test in diagnosis.

A few of the published statistics indicate both the rarity and irregular appearance of cases of chorionepithelioma. Kimbrough (1934) observed the disease twice in 8,335 confinements, Winter (1934), three cases among 8,000. Schwalm (1934) stated that in twenty-two years no patients with the disease were observed at the Berlin Charité Frauenklinik, while Eymer (1932) at the Heidelberg Frauenklinik collected nine in twenty years. St. Sommer (1934) in Prague found one in ten years among 18,000 confinements, Joravieff (1933) in the Soviet Union reported one in 26,000.

Chorionepithelioma occurs usually in multiparas. In Teacher's series the youngest patient was seventeen, the oldest fifty-five, and the average age of the group was thirty-three years. The disease occurred during the first pregnancy in only 5 per cent of this series, following the second and third in 28 per cent. Vineberg (1919) quoted Briquel's figures indicating an incidence of 47 per cent in the fourth pregnancy. In v. Szathmary's analysis (1930) of 500 patients with chorionepithelioma, the average age was thirty-four years, and 4.4 pregnancies preceded the onset; in one-third of this group the condition developed after forty in women who had had eight pregnancies. Gestations late in the childbearing period are more likely to terminate as moles, hence, the higher incidence of chorionepitheliomas in this group. Devitzky's patient (Ries, 1913) at seventy-five seems to be the oldest on record. Cases occurring in early childhood are teratomatous like the testicular type.

*Read at the Eighth Annual Meeting of the Central Association of Obstetricians and Gynecologists, Detroit, Mich., October 15 to 17, 1936.

The time relationship between the most recent pregnancy and the development of the chorionepithelioma is subject to wide variations. Coincident with intra-uterine pregnancy were the cases reported by Walthard, Gustavson, Eyding (1933), Stoeckl (1933), Jacob (1930), and most recently by Davis and Brunschwig (1936). Coexisting with an intrauterine mole were the cases of Halter (1930), Schickele, Sunde, Lehmann (cited by Halter, 1930), and Pantschenko (1931). Appearance of the tumor after the menopause has been reported by Koritschoner (de Zalka, 1928), Kroesing, McCann, Devitzky, and Polano (Ries, 1913). Feiner (1935) analyzed a number of these reports. Well-authenticated cases following a long latent period are rare in the recent literature.

Chorionepithelioma follows moles, abortions, term pregnancies and ectopic pregnancies in the order mentioned. In this, as in many other phases of this study, individual reports differ. Polak (1931) stated that in ten years he had seen 40 or 50 moles, none of them malignant, and in the same interval, 10 chorionepitheliomas without antecedent mole history. Larger series indicate that 50 per cent are preceded by moles, the others develop after term pregnancies and abortions with a slight emphasis on the latter. The high incidence of malignancy following mole, 5 per cent or more, indicates the gravity of this condition. In 1934 a total of 36 chorionepitheliomas of the fallopian tubes and an equal number of the ovary had been reported. The ectopic form has been studied carefully by Findley (1904), de Zalka (1928), and Sears (1933).

The pathology of chorionepithelioma is essentially an intensification or exaggeration of many of the growth processes of normal pregnancy. The normal chorion is a rapidly proliferating tissue with definite invasive qualities and a tendency to metastasize. When malignant, these functions are exaggerated, and diagnosis rests on the recognition of such hyperplasia. Chorionepithelioma arises from the cells of the fetal trophoblast. Both the Langhans' layer and the syncytium are involved, but rarely to the same degree. Numerous attempts have been made to classify these tumors on the basis of cellular constituents, but none of these classifications has clinical application although Ewing's seems best. Since both types of cells have a common origin there is no need of precise distinction. Predominance of either type of cell in a tumor cannot be relied on as an infallible criterion of malignancy. Recognition of the distortion of the normal processes, not always easy, is most important. Erroneous diagnoses have been made often, leading either to fatal procrastination or to unnecessary sacrifice of pelvic viscera.

The uterine tumor may consist of only a few cells or it may fill the entire pelvis. It is a hemorrhagic growth due to the invasion of blood vessels. There is no stroma, hence, no intravillous vessels, and the cells in the deeper parts of the tumor grow away from their blood supply. Both necrosis and hemorrhage thus result. The lesion may lie super-

ficially on the endometrium, within the myometrium, or project into the peritoneal cavity as a subserous mass. Some tumors have a superficial hyperplasia, while others are best exemplified by the so-called invasive mole, in which the first symptoms may be peritoneal or those due to uterine rupture. Anspach and Hoffman (1931) have reported such a tumor and have reviewed the records, citing nine other well-authenticated cases.

Histologically there are: an active hyperplasia and accumulation of the covering elements of the villi, both Langhans' layer and the syncytium; penetration of both these elements deep into the wall of the uterus; numerous Langhans' cells in mitosis; and regions of necrosis and hemorrhage. All of these conditions may not be present in the sections examined, and sometimes hemorrhage and tissue destruction dominate to the exclusion of finer details.

Chorionepithelioma in women has a decided tendency to metastasize through the blood stream, and lesions in the vaginal wall and lungs are usually the first to appear when dissemination occurs. This, of course, is a natural sequence, because the chorion even in normal pregnancy invades the uterine vessels, and, as Schmorl many years ago stated, benign embolic chorionic tissue can be demonstrated in distant viscera in fully 80 per cent of pregnancies. These facts are important in treatment. Unless there is gross evidence of extension into the parametrium, the dissection during a hysterectomy need not be as wide as when done for carcinoma, and the knowledge that pulmonary metastases may appear first should be a guide in deciding the operability of a patient and the subsequent treatment. Moreover, the blood vessel metastases urge gentleness in manipulating the uterus, as emphasized by Hitschmann.

Vaginal metastases are interesting features of this disease. This unique retrograde metastasis is attributed to anastomoses between the uterine vessels and those of the anterior vaginal wall. In about half of the patients, according to Williams, a vaginal metastasis is the first symptom. The lesions usually occur near the urethral meatus, vary from a few millimeters to several centimeters in diameter, appear superficial, are blue in color, and resemble varices. When traumatized, they bleed freely. This accident often has led to a diagnosis of the basic disease. Stroganova (1931) questioned the importance of this lesion and stated that he had observed it in other conditions. In my patients no vaginal metastases occurred.

Exceptions to the hematogenous type of dissemination have been observed.

Cases have been reported by Lutfi and Schükri (1933), who cite similar observations by Riesel and Kroemer, in which lymphatic involvement has been conspicuous. Ikeda and Ikeda (1933) report a patient with generalized involvement of the skin,

an observation which seems to have no parallel in published reports. These few instances serve only to emphasize the rarity of primary lymphatic involvement. The so-called chorionepithelioma testis metastasizes through the lymphatic system, suggesting a fundamental difference in type of tumor even though the cellular elements and biologic reactions may be indistinguishable.

As a rule, the persistence of bleeding following an abortion or the expulsion of a mole is the most common clinical symptom, and further bleeding after a curettage is almost pathognomonic. Too often, however, the microscopic examination of this material is neglected or when made does not reveal its true nature, in fact, even the myometrium of the excised uterus will often show no more than regions of necrosis and blood extravasation. The circumscribed lesion deep in the myometrium, obviously, is inaccessible to the curette. Pain is variable, and as a rule develops late in the disease; anemia usually is in proportion to the blood loss, and by increasing the operative hazard as well as lowering resistance to infection constitutes the most serious symptom. Low-grade fever, due to bacterial invasion of the uterus through a patulous cervix, is common, and severe sepsis often has prevented radical excision or caused death.

Metastatic lesions, due to their hematogenous origin, are intimately associated with the blood vessels of the tissues involved, and the symptoms they produce result from bleeding or other vascular phenomena, such as bleeding varices in the vaginal wall, hematuria, hemoptysis, etc. Cerebral lesions are frequently characterized by symptoms of increased intracranial pressure or by cranial nerve involvement.

Many patients are not observed long enough, and the development of symptoms due to metastases has finally called attention to the true nature of the condition. The seriousness of this omission has been stressed particularly by Curtis (1932). Presenting the greatest difficulties in diagnosis are the tumors which occur in the puerperium when physiologic bleeding masks the symptoms of the malignant growth, so strikingly illustrated in the reports by Lull (1935) and Winter (1934).

The hormone studies, especially the Aschheim-Zondek test and its modifications, are invaluable in the study of chorionepithelioma. So important is this test that skepticism regarding many of the older reports is aroused, particularly those recording spontaneous cures and diagnoses based entirely on the microscopic examination of curetted material. Similar reports today would be made with reluctance except when substantiated by biologic tests, because the presence of living chorion in any part of the body is manifested by the excretion of excessive quantities of anterior pituitary-like hormone. In normal pregnancies an error of 1 or 2 per cent occurs in these tests, and at

times nonpregnant women may excrete an excessive amount of the hormone. Controversy arises when the histologic structure and the Aschheim-Zondek test do not coincide.

The report of Fahlbusch (1930) is an example. The histologic diagnosis was made by Robert Meyer; the Aschheim-Zondek test, however, was negative and continued thus. No treatment was given after the curettage and the patient remained well. Mathieu and Palmer (1935) advance as a very rational explanation of these apparent discrepancies that the first urine specimen was obtained five days after the operation, and in both of their patients the Friedman test had become negative by that time. Further experience will clarify similar conflicting statements.

The biologic test should be valued, but the absence or presence of an excessive quantity of the hormone in a single specimen of urine should not outweigh clinical judgment. A repeatedly positive reaction without other symptoms has demonstrated the great value of this test (Leventhal and Saphir, 1934), and a single negative report does not exclude malignancy. Chorionic cells which develop malignant tendencies after a period of latency must have survived, and their presence may be obscured by an occasional inconsistent result. Such a variation in the intensity of the hormone reaction was shown in the patient recently reported by Garber and Young (1936), in whom chorionepithelioma developed five months after an hydatidiform mole, meanwhile two of the Friedman tests were only weakly positive. Similarly in the fourth patient of my group, all of the reactions were less strongly positive in the interval between the abortion of the mole and the hysterectomy. Persistence of a positive reaction, even though it is slight, is far more suggestive than a single one with high hormone content.

Blindly accepting the fact that the test often remains positive for several months after the expulsion of a mole (Aschheim, 1930) may lead to disaster, again illustrated by the fourth patient in my report. Malignancy seemed to be present in the chorion of the original mole, and so marked were these in the material of the second curettage that hysterectomy was urged although less than six weeks had elapsed. This opinion was substantiated by the sections which show well-developed chorionepithelioma metastasis in the myometrium.

In no other disease is prognosis dependent so much on early recognition and early treatment. An abnormal type of pregnancy by its nature warns the physician of serious sequelae, and hormone tests are done on the slightest suspicion. But when physiologic chorion becomes malignant during an otherwise uneventful pregnancy or puerperium, recognition may come too late. Numerous factors serve to overwhelm the patient, such as the confusion of symptoms with those due to the pregnancy, the anemia and lowered resistance, the tendency to metastasize through the blood stream and the dilated pelvic vessels favoring embolism. The result depends on factors beyond the control of

the physician. Further confusion is caused by variation in the degree of malignancy, some tumors appearing almost benign in their response to minor or inconsequential treatment, others produce death before their nature is suspected. The factors, apart from trauma, actually functioning in producing embolic metastases also are unknown.

A marked improvement in prognosis has resulted from the use of the Aschheim-Zondek test. In contrast with the previous mortality of 60 per cent or more is the report by Engelhart (1935). He observed five consecutive patients in the last eight years in all of whom the diagnosis and treatment were controlled by this test, and all were returned to good health. Similar reports are becoming more common.

In patients with chorionepithelioma following pregnancies not of the mole type, failure to make an early diagnosis may be fatal to the patient but this is not a reflection on the attending physician. Protracted or repeated bleeding following a confinement or abortion, however, should prompt a hormone test of the urine, and a wider use of the latter will aid in decreasing the mortality. Hydatidiform mole should be considered a potentially malignant tumor. The various criteria advanced for differentiating benign from malignant moles, while of interest, in no manner refute the simple fact that the malignant mole, regardless of its structure, precedes chorionepithelioma. The age of the patient bearing the mole may be more important than the histologic structure.

This is clearly illustrated by v. Szathmary's analysis. Under forty, mole preceded chorionepithelioma in 37.7 per cent with a mortality of 40 per cent; at age forty and over, a preceding history of mole was obtained in 68 per cent, and the death rate had mounted at forty to 74 per cent, at fifty to more than 80 per cent. This increased incidence of malignancy of the chorion in patients approaching the climacterium coincides with the same tendency in other pelvic tissues at this age. While in younger women anxious to bear children a more conservative attitude can be taken, the diagnosis of mole in a patient past forty years of age should indicate hysterectomy.

When chorionepithelioma has been diagnosed, prompt complete excision of the tissues involved is the ideal treatment. Anemia should be combated by transfusion before the operation. Abdominal hysterectomy is the operation of choice, permitting better exposure, the ligation of vessels before clamping and cutting, and the removal of the uterus with the least trauma, as well as assuring better hemostasis. The lutein cysts of the ovary are due to the disease and have no causative significance, hence, removal or conservation of the ovaries is optional. The excision of tissue-containing malignant cells, however, would naturally take precedence over the conservation of ovarian function. The cervix should, of course, be removed.

There are relatively few reports in English of primary irradiation in the treatment of chorionepithelioma, its use being restricted largely to inoperable cases or to those with metastases.

The excellent results obtained by Davis and Brunshwig (1936), Lackner and Leventhal (1932), Beach (1934), and Thomas (1934) indicate the value of this form of therapy. The German literature is more voluminous and contains a number of excellent reports, some authors having used x-ray alone and others combining it with radium. Wintz's (1931) report is particularly impressive; of 9 patients, all considered serious, treated by irradiation alone, 7 were cured. Gál (1933) lists the advantages of irradiation therapy as the avoidance of bleeding, infection, and the mechanical dissemination of metastases. Certainly in the inoperable patient and when the surgical risk is great, irradiation has proved valuable. Further experience may justify an extension of this form of treatment.

The following five reports are the records of the only cases of chorionepithelioma observed at St. Luke's Hospital, Chicago. Among the case histories of this institution there are two more in which the diagnosis clinically and histologically justifies their inclusion, but inability to make further contact with these patients has necessitated their omission. It will be noted that the diagnosis had not been made prior to 1929, but during the following year two cases were observed and since then three more have been studied. Since these occurrences coincide with what may be called a transition period in the diagnosis of this disease, a recital of our case histories will illustrate the value of the Aschheim-Zondek test.

The tissue examinations were made by Dr. Edwin F. Hirsch, Attending Pathologist at St. Luke's Hospital. The finer discriminations in histologic structure essential in the diagnosis of this condition are not within the province of the clinician.

The biologic tests were made by Dr. William Tate, Jr., using the modification of the original Aschheim-Zondek technic described by Davis and Ferrill (1932). Albino rats twenty-five to thirty days old and weighing 40 to 50 gm. were used. The test may be made with either male or female animals, but in this series females were used exclusively. Four intraperitoneal injections of 2 c.c. of urine were given at twelve-hour intervals, and the animals sacrificed forty-eight to seventy-two hours later. This technic has been entirely satisfactory in the routine performance of pregnancy tests. The quantity of urine used is somewhat larger than is necessary to elicit a reaction in normal pregnancy, but the reading is easily made and is attended by only a small error. From an economic standpoint, in the avoidance of questionable reactions, and for the greater detail obtained in his studies of early pregnancies, Dr. Tate prefers rats to either mice or rabbits.

CASE HISTORIES

CASE 1.—F. De J., a white woman aged thirty-eight years and married for one year, had been well until four months before entering St. Luke's Hospital Dec. 26, 1929. After several weeks of amenorrhea and sudden metrorrhagia, her physician, Dr. C. W. Barrett, in August, 1929, had curetted the uterus and discovered an hydatidiform mole. There were no symptoms for a month and then bleeding recurred. It was slight but almost constant; menstruation, however, occurred regu-

larly each month. There had been no other pregnancies. The urine contained 5 mg. of albumin per 100 c.c. On Dec. 27, 1929, the supravaginal portion of the uterus and the appendix vermiformis were removed by Dr. Barrett.

The uterus amputated through the cervix 2 to 3 cm. below the internal os was 7.5 cm. long. It had been split to the cavum lengthwise in the posterior mid-sagittal plane. Near the vertex on the anterior wall, closely attached, was a tough gray tissue with small vesicles 2.2 by 2.0 cm. elevated 0.7 cm. In the muscle beneath were several other vesicles 7 to 8 mm. in diameter. In the anterior wall toward the right cornu another section had been made down to the mass mentioned, and in this tract was a vesicle 2.2 by 1.5 by 1.7 cm. At the periphery, a channel 5 to 6 mm. in diameter extended to the amputation of the broad ligament. Dr. Barrett stated that another vesicle had been found in this sinus, and, in fact, a collapsed structure 1.2 cm. in diameter was present. The wall of the uterus in its posterior mid-sagittal plane was 1.8 cm. thick, and 1 mm. of this was hyperemic lining. The lining of the upper part of the cervix had the usual arbor vitae markings.

Sections were cut so as to include the myometrium and the mass of tissue adherent to the lining surface. The muscle contained several large blood vessels with

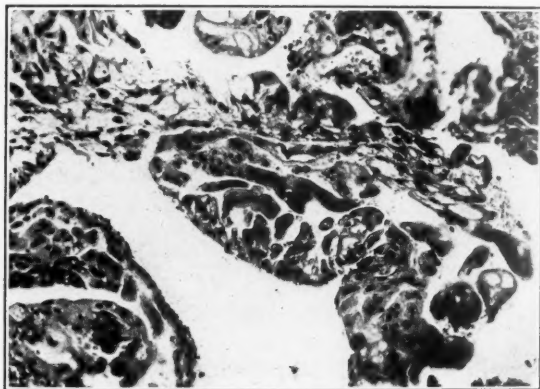


Fig. 1.—Photomicrograph of a metastasis in the lumen of a blood vessel. $\times 212$

thick walls surrounded by a zone of fibrous tissue. About some of the blood vessels were small collections of lymphocytes and a few polynuclear leucocytes. The mass protruding into the cavum was continuous with the dense fibrous tissue and large blood vessels. It had a fibrous stroma and a variety of large swollen cells, some resembling huge decidua cells, bizarre chorionic villi with a compact fibrous stroma, Langhans' cells and syncytial cells. There was a hyperplasia of the syncytium into irregular multinuclear protoplasmic masses. In the lumen of a large blood vessel, as seen in Fig. 1, were masses of these syncytial cells, and large solitary cells had penetrated the intima and media of some of the blood vessels.

The patient recovered promptly from the operation and has remained well. The Aschheim-Zondek tests to date have been negative.

CASE 2.—M. W., a negress, aged twenty-three years, entered the hospital on the service of Dr. H. O. Jones on Nov. 19, 1929. She was married at the age of fourteen, and had been delivered twice, seven and six years before. The last menstrual period was April 24, 1929; during the latter part of June there had been slight vaginal bleeding, and on the first of July she aborted spontaneously. From then until admitted there had been a slight continuous bleeding. There were moderate secondary anemia, a temperature of 99.6° F., and a pulse of 108 per minute when she

was admitted. The left Bartholinian gland was palpable, the uterus was enlarged to three times its normal size, and the cervix was widely patulous. After a week in bed she was curetted.

The small amount of tissue recovered included masses of red blood cells, fibrin, traumatized endometrium, and some myometrium. Among the tissue fragments were chorionic villi and masses of syncytium. There was a chronic inflammation of the endometrium.



Fig. 2.—Patient 2. The fundic portion of the uterus opened in the mid-sagittal plane. Note the hemorrhagic necrotic nature of the tumor in the vertex.

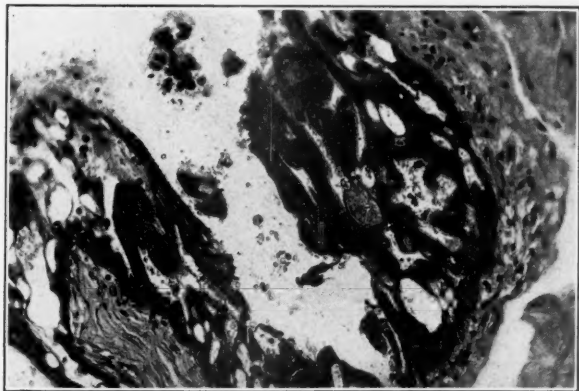


Fig. 3.—A photomicrograph of the tumor in Fig. 2, illustrating a mass of tumor cells in one of the irregular tissue spaces. $\times 212$

She was discharged from the hospital Nov. 30, 1929, and did not return to the dispensary until Jan. 20, 1930, and then not again until March 10. At both times she was urged to enter the hospital for further treatment of the persistent bleeding. She finally came to the hospital on March 30, 1930. She had no fever, and the pelvic conditions were essentially the same as in the previous November. The uterus was slightly smaller. There was a moderate anemia, the leucocytes were

6,050 per c.mm., and the hemoglobin was 52 per cent. On March 20, 1930, four months after the curettage, and nine months after the abortion, the supravaginal portion only of the uterus was removed.

The upper 6 cm. of the uterus including 3 cm. of the cavum had been cut to the lumen in the mid-sagittal plane (Fig. 2); the wall here was 3.3 cm. thick, and of this, 3 mm. was endometrium. The peritoneum was smooth and glistening. Intramural in the vertex was a circumscribed mass of tissue 4.5 by 3.5 by 4.5 cm., which, on surfaces made by cutting, contained several large dark red blood clots. In some respects it resembled an extremely hemorrhagic fibromyoma, but the fibrous-like stroma formed a porous framework with tissue spaces about 1 cm. in diameter filled with blood clots. The histologic preparations contained many red blood cells and fibrin, and, as shown in Fig. 3, chorionic villi covered with irregular masses of syncytium. The tissue structure was that of a chorionepithelioma.

The patient was discharged from the hospital on April 17, 1930. On May 18, there was a small hemorrhage, but pelvic examination disclosed no unusual conditions. When seen in the dispensary in June and again on August 4, she seemed well. About the middle of September she had several headaches, and, on one occasion, diplopia. A complete neurologic examination on September 29, however, revealed only normal findings.

During the next few weeks many symptoms developed, and on Oct. 22, 1930, she was admitted to the hospital for the fourth time. The headaches, localized in the left occipital region, had become constant. There were considerable precordial pain and dyspnea, anorexia, vomiting, increasing weakness, and discomfort. The hemoglobin had decreased to 36 per cent, the red cells to 2,240,000. Pelvic examination by Dr. Jones was entirely negative, and neurologic examination by Dr. George W. Hall as late as November 5 revealed no organic changes. An examination of the eyes by Dr. Frank Brawley was negative for evidence of intracranial disease. The urine was normal.

Roentgen films of the chest revealed a mass in the right posterior mediastinum not present at the time of the examination in April, and diagnosed as a metastatic lesion. On October 29, an examination of the skull disclosed a number of regions of increased radiability of the cranial bones, which, in view of the history, were considered compatible with metastatic malignant growths. The sella was within normal limits, and there was no evidence of increased intracranial pressure. Roentgen treatments to the chest were given on November 14 and 15.

During the last few days the patient failed rapidly and numerous metastases occurred in the chest and abdomen. She was discharged from the hospital November 18, because she was unwilling to remain longer away from her children.

Death occurred at home on December 21, 1930. Permission for an autopsy was refused.

CASE 3.—N. McM., a negress aged twenty-nine years, and married for nine years, had two children, four and six years of age. In August, 1930, she had a spontaneous miscarriage of a three months' pregnancy. For a short time after this she had a moderate metrorrhagia. Then followed normal menstrual periods on October 1 and November 5. From December 8 to 31 she had metrorrhagia two to four days and corresponding intervals without. A large blood clot was passed on December 31. When admitted to St. Luke's Hospital on Jan. 3, 1931, her temperature was 101.8° F., pulse 132, and her blood pressure was 88/30. The external os was dilated 2 cm., and from the opening protruded a mass of friable tissue. The corpus was soft and enlarged to the size of a uterus in the third month of pregnancy. The clinical diagnosis was abortion. There was a marked secondary anemia, and a transfusion

of 610 c.c. of blood was given. The uterus was curetted and the tissue removed, illustrated in Fig. 4, was reported as chorionepithelioma. Dr. H. O. Jones removed the uterus and both tubes and ovaries on Jan. 14, 1931.

In the lining of the center of the anterior wall, 1.5 cm. above the level of the internal os, there was a slightly elevated mass of tissue with a roughened surface that extended to a depth of 1 cm. In the center of this was a hemorrhagic necrotic region 7 mm. in diameter. Another yellow hemorrhagic nodule at the same level on the right side nearby was 8 mm. in diameter. This was continuous in the wall with the first and extended 1 cm. into the muscle. There were no gross changes of the ovaries or fallopian tubes. The nodules contained much hyalin scar tissue and organizing granulation tissues with scattered large solitary syncytial cells. Several large blood vessels with thick hyalin fibrous walls were present in the scar tissue and in the wall of one of these was a large solitary cell in mitosis.

The Aschheim-Zondek test reported on Jan. 24, 1931, was strongly positive. Two roentgen treatments were given, and the patient was discharged from the hospital on the twenty-first day after her operation. During the next three months six more

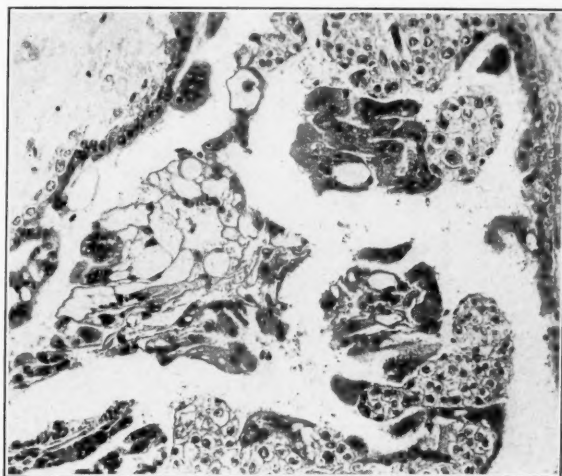


Fig. 4.—Curetting from Patient 3, illustrating the irregular masses of chorion, the atypical arrangement of the syncytium and Langhans' layer. $\times 160$

treatments were given. She has remained under observation in the dispensary clinic. The Aschheim-Zondek tests have been negative since she left the hospital. She has no signs or symptoms of metastases.

CASE 4.—H. H., a white woman aged thirty-two years, came under my care on Dec. 6, 1935. Nine years before she had aborted spontaneously in the sixth month of her first pregnancy. Two years later she was delivered at term. Her last menstrual period occurred Oct. 12, 1935, and for a week before consulting me she had had a slight continuous metrorrhagia. The external os was contracted and the uterus was enlarged to the size of an eight weeks' pregnancy. The blood pressure was 114 systolic and 70 diastolic. Metrorrhagia continued for a month although the patient remained in bed. On Jan. 5, 1936, twelve weeks after the last menstrual period, the fundus of the uterus was at the navel and was moderately soft. During the next five days the uterus increased to even greater size and its contour was irregular. Hydatidiform mole was diagnosed clinically. Urine collected during the day and diluted with an equal volume of water produced a strongly

positive Aschheim-Zondek reaction. The blood pressure had risen to 158 systolic and 98 diastolic. The fundus of the uterus was 17 cm. above the symphysis pubis and 14 cm. wide.

On Jan. 15, 1936, the cervix was dilated and about 1,200 c.c. of hydatid tissue were removed. The histologic examination of this tissue disclosed a hyperplasia of the syncytium and Langhans' cells. The hyperplasia of the syncytium along the margins of the villi suggested the possibility that any tissue remaining in the uterus would continue to grow, and therefore the patient should be kept under close observation for recurrence. There was a moderate secondary anemia; the blood pressure gradually returned to 100 systolic and 70 diastolic. The urine on January 15 produced marked second and third phase Aschheim-Zondek reactions in rats in dilutions up to 1:32, and occasional hemorrhagic follicles above this dilution. The patient left the hospital on January 19.

The Aschheim-Zondek tests each week were strongly positive. The uterus on January 30 was about twice the usual size, and a slight metrorrhagia persisted. After a severe hemorrhage on February 21 the patient returned to the hospital, and

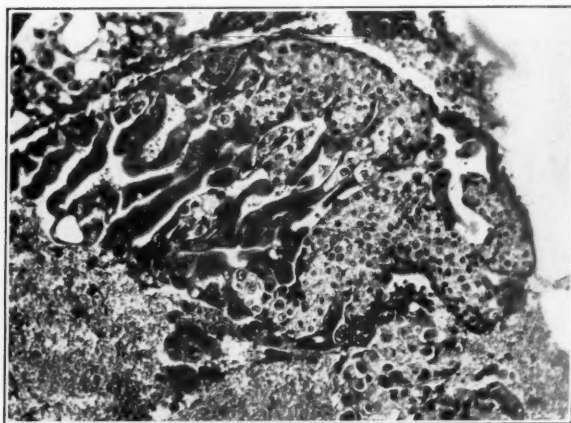


Fig. 5.—Patient 4. Photomicrograph of material obtained at the time of the second curettage. The marked atypical hyperplasia of the chorionic tissues is clearly illustrated. Hysterectomy was urged after viewing this section. $\times 198$

for twelve hours the uterus was packed. Some tissue obtained at this time contained masses of syncytium, trophoblastic cells, large solitary cells with bizarre nuclei, and a few vesicles. In Fig. 5 a typical field is reproduced. On Feb. 28, 1936, forty-four days after the first curettage, the entire uterus and both tubes and ovaries were removed.

The uterus was 11 cm. long and 7 by 5 cm. between the horns. The wall in the anterior mid-sagittal plane was 3 cm. thick. The myometrium was edematous and had many large blood spaces. The lining was granular and hemorrhagic because of the recent curettage. On the left side anteriorly was a mass of soft red brown tissue 3 by 2.5 cm. and 0.5 cm. thick. After the uterus had been hardened in fixing solutions, several segments 2 to 4 mm. thick were cut through and near this mass of red brown tissue. At a level 1.5 cm. below the lining, deep in the muscle of the left side was a hemorrhagic tissue 1.5 cm. in diameter (Fig. 6). Histologic preparations of this nodule contained hemorrhagic necrotic tissue, masses of large solitary cells, and chorionic villi with hyperplasia of the trophoblastic and syncytial cells; a typical microscopic field is shown in Fig. 7.

Before the operation the patient was given a transfusion of 400 c.c. of citrated blood, and this was repeated one week later. After an uneventful convalescence she was discharged from the hospital sixteen days after the hysterectomy. The Aschheim-Zondek test was negative on the thirteenth day and has remained so since. The patient is well.

CASE 5.—C. K., a white woman aged forty, entered the service of Dr. G. C. Finola at St. Luke's Hospital on Feb. 28, 1936, for the care of her third pregnancy. The other pregnancies had terminated at full term fifteen and nine years before. The last menstruation was Oct. 7, 1935, and during the last part of December she had

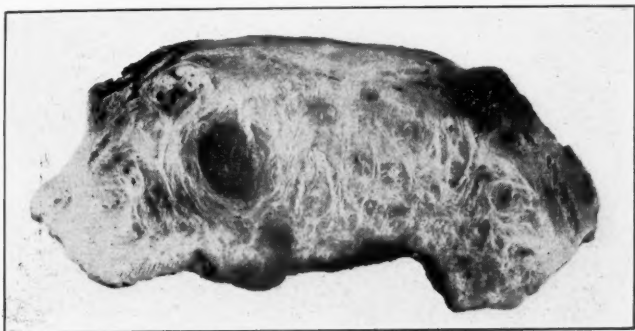


Fig. 6.—Photomicrograph of a metastasis 1.5 cm. in diameter in the myometrium. Patient 4.

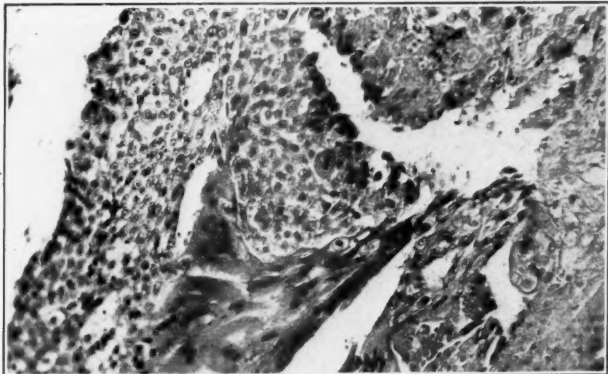


Fig. 7.—Photomicrograph illustrating the tissues in the metastasis in the myometrium. Patient 4. $\times 212$

slight metrorrhagia which continued until she entered the hospital. She had not felt any fetal movements, her systolic blood pressure was 184 and the diastolic, 108. The uterus was enlarged to the size of a four months' pregnancy. Therapeutic abortion was indicated because of the patient's age, the high blood pressure, and the metrorrhagia. The uterus was emptied of a large hydatidiform mole on Feb. 28, 1936.

In the histologic preparations there was a marked hyperplasia of the Langhans' and syncytial cells covering the vesicles, and among the cells were many in mitosis (Fig. 8). The Aschheim-Zondek test was positive in a 1:32 dilution of the urine.

The uterus, both tubes and ovaries were removed on March 6, 1936. The pear-shaped uterus was 14 cm. long, and about 10 cm. wide, and 6 cm. thick between the horns. In the anterior mid-sagittal plane the wall of the body of the uterus was 2.2 cm. thick. The lining surface was rough. Closely adherent in the left cornu was a mass of red brown tissue 7 cm. long, 6 cm. wide, and 3.5 cm. thick. Histologic preparations of this contained masses of red blood cells, fibrin, and necrotic vesicle

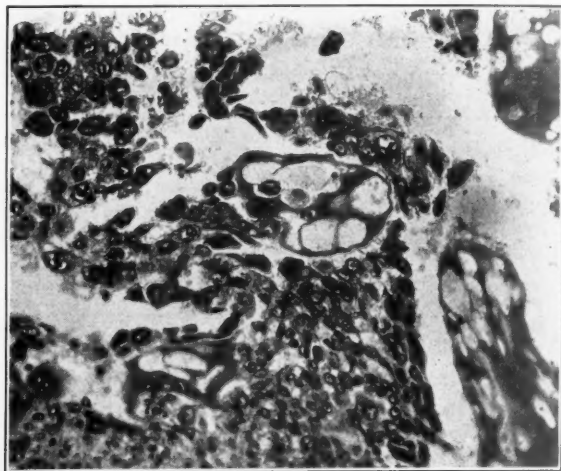


Fig. 8.—Mole tissue curetted from the uterus of Patient 5. Note the marked cellular proliferation and the irregular arrangement of the cells. $\times 212$

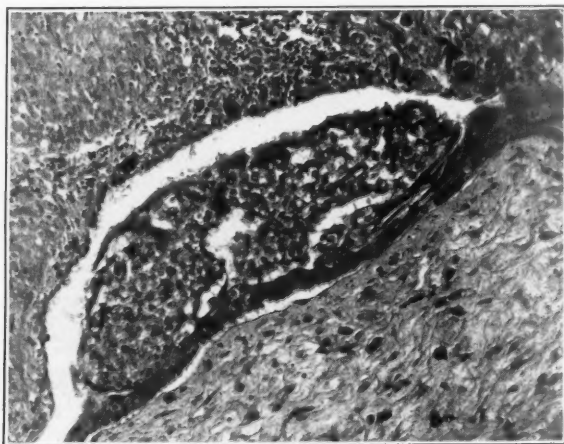


Fig. 9.—Photomicrograph of a villus invading a blood vessel in the myometrium. Patient 5. $\times 212$

mole tissue. The deeper tissues included endometrium with many large solitary syncytial cells and adjacent myometrium also invaded by these tissue elements. In Fig. 9, a well-localized metastasis is shown. Masses of unorganized syncytial and trophoblastic cells were found in the necrotic tissues along the caval edge.

The postoperative course was uneventful. The patient left the hospital fourteen days after the operation. The Aschheim-Zondek test on the day of the hysterectomy

was strongly positive in a dilution of 1:32; on March 13, one week after the operation, it was entirely negative, as it has remained at monthly intervals since. The patient is in excellent health.

SUMMARY

During the last seven years 5 patients with chorionepithelioma have been observed. In this group the average age was 32.4 years, the youngest was twenty-three, the oldest forty. Three patients were white women and 2 were negroes. In 3 cases the preceding pregnancy was an hydatidiform mole and 2 followed spontaneous abortions. The 2 patients observed before the interruption of the mole pregnancy showed the hypertensive type of toxemia frequently associated with this condition.

The common symptom was metrorrhagia, and this persisted from six weeks to nine months before the cause was determined. Except in the third patient, no definite latent period intervened between the pregnancy and the chorionepithelioma. In the second patient bleeding persisted from the time of the abortion until metastases had developed.

Abdominal hysterectomies were done on all these patients. In 2 only the corpus was excised and in both of these the ovaries were conserved. The last 3 had complete hysterectomies and the adnexa were also removed. Our experience with roentgen therapy has been too limited to justify conclusions.

The one fatality is attributed to the delay in diagnosis so common before the use of the hormone tests. The importance of the latter in the diagnosis of chorionepithelioma is so well established that further comment here seems unnecessary except to emphasize its newness. Such a test was not available when the first patients in this series were observed.

Among the reported cases there have been few diagnostic errors ascribable to these tests, their great usefulness in the detection of malignancy of the chorion has been amply proved. No test, however, can replace clinical judgment, and the value of this agent is dependent on the proper selection of patients; the laboratory report must be interpreted in the light of the clinical history.

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DISCUSSION

DR. THOMAS B. SELLERS, NEW ORLEANS, LA.—The records of the private hospital in which I work show an incidence of 6 cases in 4,631 pregnancies during the last ten years. One case followed or complicated hydatid mole. This is a general surgical hospital, about 80 per cent of the work being surgery.

I personally reported one case of chorionepithelioma with hydatid mole in 1923. After removal of the mole the physical condition of the patient was such that hysterectomy would have been a hazardous procedure; therefore radium was used, complete hysterectomy being performed later. A recent report on the condition of the patient shows that she has had no recurrence or complication.

Dr. Gough has already mentioned the difficulty of diagnosing these cases. Inasmuch as an error in diagnosis means a fatal result, more frequent use of the Aschheim-Zondek test is indicated in the presence of histories suspicious of chorionepithelioma.

Emphasis should also be placed upon the importance of complete hysterectomy in these cases.

DR. FRANK W. SMYTHE, MEMPHIS, TENN.—I personally have had experience with chorionepithelioma on only two occasions. Since that time I have had four cases which, while the scrapings were not definite, were extremely suspicious. After hysterectomy in these four cases we found they were placentoma. I would like to ask one question: What value, if any, has the Aschheim-Zondek test in placentoma as compared to chorionepithelioma?

DR. RALPH LUIKART, OMAHA, NEB.—I believe that in a case with a positive Aschheim-Zondek one month postpartum which increases in the strength of the reaction for two months, there is no excuse for further delay in removal of the uterus. All such cases with prolonged positive Aschheim-Zondek tests associated with hydatidiform mole can be saved from chorionepithelioma if properly handled. I would like to have the essayist state why he delayed operation in his case with a prolonged positive Aschheim-Zondek test.

DR. WILLIAM T. BLACK, MEMPHIS, TENN.—It would be interesting to know why under certain circumstances the chorionic epithelial cells continue to proliferate and produce one of the most virulent types of malignancy. Langhans' cells have been found during a normal pregnancy in the lungs, liver, kidney, and other organs, yet these do not usually take on malignant characteristics. There is evidently present during normal pregnancy antibodies or some lytic substance that takes care of these

cells. However, as Blair-Bell and others have taught there is under certain circumstances after the death of the fetus and under other conditions, a loss of resistance, and these embryonic cells grow locally and metastasize rapidly to other organs.

A few years ago the speaker reported six cases of chorionepithelioma that occurred in Memphis. While it has been stated by several of the best authorities that chorionepitheliomas follow moles in more than 45 per cent of the cases, it has been shown by Novak, Meyer, and others that chorionepithelioma does not develop after moles in over 1 per cent of cases. In only one case out of the six I have just noted did the chorionepithelioma follow a mole.

Any woman who has a prolonged bleeding after pregnancy should have an Aschheim-Zondek test, and if this is positive, she should have a diagnostic curettage performed. While most of these prove to be placentomas, one will occasionally find the most malignant chorionepithelioma.

DR. ALFRED J. KOBAK, CHICAGO.—The possibility of early diagnosis after expulsion of a mole by the use of the modified Aschheim-Zondek test is a step forward in the early diagnosis of chorionepithelioma. I would, however, like to raise the question of the limitations of the test in the early diagnosis of chorionepithelioma. I had one case where a hydatid mole was expelled and about six weeks after there was a high concentration of hormone in the urine. It proved to be a normal pregnancy. There have been cases in the literature where with the expulsion of a hydatid mole the urine shows no hormonal content and the Aschheim-Zondek test is negative. At the Tumor Clinic of the Michael Reese Hospital I have been shown slides of a synecioma, in which the preoperative hormonal tests were negative. I would like, therefore, to raise these questions: If we do find a positive test, shown by a high hormonal content of the urine, must we invariably conclude that the patient has chorionepithelioma? On the other hand, if we have a negative test are we safe in concluding that the patient has none? I believe these questions will be answered when more people report their negative findings.

DR. HENRY E. KLEINBERG, DES MOINES, IOWA.—In a recent case of mine of hydatidiform mole expelled at three months, the Friedman test became negative after one month. Since then we have done one more Friedman test and several skin tests with APL, which have all been negative. I feel, however, that this case should be followed for two, three, or four years, because some little piece may be present without giving the hormonal reaction, and it is possible that this area may become malignant later on.

DR. ROLAND S. CRON, MILWAUKEE, WIS.—In a recent case of mine, suspected of having a chorionepithelioma, following an abortion, sections of curettings from a 4 cm. nodule in the right broad ligament showed no evidence of tumor. The hormonal test at that time gave a weakly positive reaction, for only one ovary in each rabbit injected showed any sign of follicle ripening even though undiluted and diluted specimens of urine were subsequently used. This patient developed sepsis following removal of the tissue from the broad ligament with very brisk uncontrollable hemorrhage. Death occurred at the end of about eight days. The lesson to learn from this particular case is that one should use x-ray therapy because it is the only method of saving the patient's life. At autopsy chorionepithelioma nodules were found in the lung.

In another patient operated upon for hydatid mole, chorionepithelioma was found in the uterus. Friedman tests taken before removal of the uterus were entirely negative.

DR. GOUGH (closing).—In the fourth patient, the delay between the first curettage and the hysterectomy in the presence of a persistently positive Aschheim-

Zondek reaction was due to conservatism. Aschheim in his article in THE AMERICAN JOURNAL OF OBSTETRICS AND GYNECOLOGY in 1930 stated that the reaction may remain positive for several months after the expulsion of a mole. Several other authors have concurred in this statement, and have thus obscured the fact that chorionepithelioma may develop in the interim or actually coexist with the mole. One should not complacently accept a positive Aschheim-Zondek reaction as a normal sequel persisting for many weeks after a mole pregnancy.

The importance of the test in the follow-up of any hydatidiform mole cannot be overemphasized. After such a pregnancy, the test should be done at least once a month, in the first month or two, even once a week. Do not be content with one or even several negative results. As an illustration, I refer to the patient reported by Garber and Young in whom a chorionepithelioma developed while a number of Friedman tests were only weakly positive.

TUBERCULOSIS AND PREGNANCY*

G. D. ROYSTON, M.D., JULIUS JENSEN, M.D., AND H. HAUPTMAN, M.D.,
ST. LOUIS, MO.

*(From the Department of Obstetrics and Gynecology, Washington
University Medical School)*

EARLY in this century, it was commonly assumed that pregnancy as a complication of tuberculosis was so serious that it required immediate interference. Schauta's dictum, that pregnancy in a tuberculous woman called for interruption, gained wide acceptance and is still followed in certain quarters. The drawbacks of childbearing in tuberculous women are obvious. The pregnancy places a strain upon the mother and so does labor. Lactation, besides being a strain on the woman, entails danger of contagion to the infant. Above all, the rearing of children with its added domestic and financial demands is certainly not conducive to the most favorable management of a tuberculous case; it has been justly said that a baby in the home is a greater danger than a baby in the uterus. These are some of the reasons against childbearing in tuberculous women, and they are potent enough to justify the statement that pregnancy should not be undertaken when there is danger that it may be complicated by active tuberculosis. A more lenient view may be undertaken when the tuberculous process is thoroughly arrested. Another problem is: what to do if a tuberculous woman becomes pregnant. This is where an increasing conservatism is gaining ground. Many women with tuberculosis pass through pregnancy and labor apparently unharmed, and when the disease takes an unfavorable turn, it is not possible with certainty to ascribe this turn to the pregnancy. No experiment or clinical evidence shows conclusively that a tuberculous process is affected beneficially or adversely by pregnancy. In recent years, the

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profession has manifested a growing interest in this subject, and closer study has resulted in increasing reluctance to interfere with the pregnancy. Follow-up studies have failed to show that the later fate of tuberculous women (excepting, perhaps, those having the serious caseous-pneumonic type of lesion) was affected by childbirth (Barnes and Barnes, Garshell, Ornstein and Kovnet). Also, if children of tuberculous mothers are carried to term, they are usually born healthy. There is little evidence that premature emptying of the uterus benefits a tuberculous woman, especially when the pregnancy becomes advanced. Some tuberculosis is likely to progress in spite of any measures that may be undertaken. The result has been an upward trend toward a more conservative attitude on the part of the medical profession, especially if the tuberculous process appeared to be arrested. The present study is a small contribution attempting to test the justification of such a stand.

MATERIAL

Fifty-one cases of pulmonary tuberculosis seen at the St. Louis Maternity Hospital during the years 1929 to 1933 were tabulated and analyzed. An additional seven patients probably also had tuberculosis, but the diagnosis could not be established beyond a reasonable doubt. Unless the disease is advanced or tubercle bacilli are found in the sputum, the diagnosis of pulmonary tuberculosis must remain largely a matter of judgment. These records were largely evaluated according to the criteria established by the Trudeau Sanatorium.* Some cases were accepted on the basis of previous opinions of some of the leading tuberculosis specialists in St. Louis. Thus, probably every advanced and moderately advanced case is included, though some latent and early cases may not have been discovered during the routine physical examination. The patients were admitted to the St. Louis Maternity Hospital either through their private physicians or through the Washington University clinics. Some, again, were referred to the University clinic from the St. Louis Municipal prenatal clinics which possess no special obstetric medical clinic. Thus, this material was drawn from an ill-defined field, from which it is impossible to obtain the total number of admitted patients, and where the thoroughness with which the patients were examined for tuberculosis must have varied. Thus, an estimate of the incidence of tuberculosis

*The criteria for the diagnosis of tuberculosis at Trudeau Sanatorium are:

1. History or presence of pleurisy with effusion.
 2. History of hemoptysis (1 dr. or more).
 3. Presence of moderately coarse râles above the third rib and the third vertebral spine.
 4. Parenchymatous change demonstrable by x-ray above the third rib and the third vertebral spine.
 5. Presence of tubercle bacilli in the sputum.
- One or more of these findings is necessary for a positive diagnosis.
All must be absent to exclude tuberculosis.

among pregnant women on the basis of this material cannot be very accurate. Additional information regarding some of these patients was graciously supplied by St. Louis City Hospital No. 2, Mount St. Rose, and Robert Koch Sanatorium. It was not possible to follow the cases beyond the puerperium; thus the material was seriously impaired.

INCIDENCE

From 1929 to 1934, 10,900 patients were admitted to St. Louis Maternity Hospital and 2,664 were delivered on the out-patient service, a total of 13,570. With 51 tuberculous cases, the incidence was 0.375 per cent. This figure is small considering the estimated incidence of tuberculosis in the general population and the fact that some of these 51 patients were referred from elsewhere because they had tuberculosis and thus would not fairly contribute to a computation of incidence. It is not probable that any considerable number of cases with developed tuberculosis has been overlooked.

DIAGNOSIS

In a pregnant woman, the diagnosis of tuberculosis frequently offers great difficulty. The more important signs were found only in a certain number of the cases. Tubercle bacilli were found in the sputum in 13 cases, hemoptysis in 19, but in 12 of these it was slight and in only one was it very severe. Cough was present in 24 but in 18 it was listed as being slight; in only 2 was it severe. Thirteen gave a past history of pleurisy. Up to the time of delivery, fever was not common. In only 15 cases was it noted and in none of these was it very marked. Persistent râles and other marked physical changes were found in 22 cases; in 22 the findings were doubtful. Excepting cases of advanced tuberculosis, interpretation of x-ray films caused much difficulty. Many persons who are not clinically suffering from tuberculosis present on x-ray examination findings suggestive of this infection. Thus, x-ray findings must be interpreted with as much care as most other single pieces of evidence. In the present series, cavitation was seen in 3 cases, in 34 the x-ray findings were strongly suggestive, in 13 they were indeterminate. In only one case did the examination fail to show changes. Thus, while it is possible that some patients have been included in this series who did not have tuberculosis, these are probably very few, partly because of the strict criteria and also because the total number of cases was proportionately so small.

CLINICAL COURSE

On the whole, the clinical course was favorable. Only 2 patients died, 3 became definitely worse, 2 showed some aggravation of the disease: a total of 7 of the 51 patients became worse during pregnancy.

Theoretically, pregnancy may have three possible effects on the tuberculous process:

1. It may increase the immune powers of the patient; this view is supported by the facts that pregnancy increases the immunity against certain other infections and that many tuberculous women feel particularly well during pregnancy.

TABLE I. COURSE OF TUBERCULOSIS IN PREGNANCY

Declined	2
Definitely worse	3
Died	2
Worse	7
Not affected	44

2. The strain of pregnancy may be too much for the tuberculous patient and result in a breakdown of her resistance. In favor of this view are the observed cases of aggravation of the tuberculosis during pregnancy, but this has not been proved to occur more frequently than would be expected among nonpregnant women. The duration of symptoms among the present group offers another point in support of this second view. While no information was available in 16 cases and 5 patients had no symptoms, 20 of the remaining 30 patients gave a history of having had symptoms six months or less. Most of these patients were seen in the second half of pregnancy, which makes it appear that in 40 per cent of the entire series and in 66 per cent of those in which the duration of symptoms was noted it is probable that these appeared after the onset of pregnancy. While neither the number nor the nature of the present material permits conclusions on this point, it at least suggests that pregnancy may be an activating factor in cases of latent tuberculosis. Of the other 10 cases, 3 had had symptoms between seven and twelve months, 1 between one and two years and 6 over two years. On the other hand, there is no evidence to show that pregnancy increases the usual liability of tuberculosis to become more severe.

3. Pregnancy might in no way affect the tuberculous process and the observed changes might be coincidental. So far, the accumulated evidence is insufficient to decide this question.

TABLE II. DURATION OF SYMPTOMS

DURATION	NO SYMPTOMS	0-6 MONTHS	7-12 MONTHS	1-2 YEARS	2+ YEARS	NO INFORMATION
Cases	5	20	3	1	6	16

In many cases, the symptoms had developed recently, possibly after the onset of pregnancy.

THE EFFECT OF TUBERCULOSIS ON PREGNANCY

One case was seen only during pregnancy and could not be traced. Thirty-eight patients went to term and spontaneous labor. In 8 of these, the weight of the child was not stated; the average weight in the remaining 31 patients was 3,340 gm., which would indicate that the tuberculous process had had no effect on the infants of these patients. One of these children was stillborn; it weighed 4,000 gm. and the mother had, in addition, toxemia. Of the 12 patients who did not have spontaneous labor at term, one was delivered at term by cesarean

section and sterilized because of the tuberculosis. Only two labors were prematurely induced, one at three and one at four months. Both were private cases. This illustrates the conservative stand of the profession. Of the 9 cases which ended spontaneously before term, two patients miscarried at two months, one at three months, one at six months, four at seven months and one patient died when five months pregnant. Considering that many of these patients had fever, the results cannot be considered unfavorable.

TABLE III. COURSE OF PREGNANCY IN TUBERCULOSIS

		Spontaneous	9
Premature deliveries----	12	Induced	2
		Cesarean	1
Normal deliveries at term----	39		
Average weight of 31 babies----	3316	grams	

ETIOLOGIC FACTORS

Tuberculosis was twice as common among ward patients as among private patients. There were 4,113 private patients and 9,457 ward patients or a ratio of 1 to 2.3. Among the private cases, 9 had tuberculosis against 42 ward patients, or a ratio of 1 to 4.7. A history of contact cannot easily be gathered from old records. Of these 51 cases, there was no mention of contact or family incidence in 36 but in 12 there was tuberculosis in parent, sister, brother, or child, and in 3 more there was tuberculosis in grandparent, uncle, or cousin.

Tuberculosis prevails in the colored race. Among the 6,111 admissions to the St. Louis Maternity Hospital for 1932 to 1935 inclusive, there were 1,348 colored patients or a ratio of 1 to 4.5. Among the 51 patients with tuberculosis, 19 were colored, a ratio of 1 to 2.7.

TABLE IV. INCIDENCE OF COLORED PATIENTS AMONG TUBERCULOUS PATIENTS. ST. LOUIS MATERNITY HOSPITAL 1932-35

TOTAL CASES			TUBERCULOUS CASES		
Colored	1348	= 22.1%	Colored	19	= 37.3%
Total	6111		Total	51	

TABLE V. AGE INCIDENCE AMONG TUBERCULOUS PREGNANT WOMEN

1. Control (Lundh and Wachenfeldt)		
24 years or less	5910	= 29.6%
Total	19621	
2. Tuberculosis (our series)		
24 years or less	19	= 37.3%
Total	51	

Norris and Landis found that the incidence of tuberculosis is especially high among women aged fifteen to twenty-five years. They associated this finding with the occurrence of first pregnancies at this time. Among the total of 19,621 cases analyzed by Lundh and Wachenfeldt, there were 5,910 aged twenty-four years or less, 29.6 per cent. Among the present 51 patients, 19 were aged twenty-four years

or less, 37.2 per cent. From these figures it would appear that the incidence of tuberculosis is high in young women. Among Wachenfeldt's 26,481 cases, 11,378 were primigravidas, 42.9 per cent. Among the present 51 cases, 18 or 35.3 per cent were primigravidas. Thus, this material does not support Norris and Landis' assumption.

TABLE VI. PARITY AMONG TUBERCULOUS PREGNANT WOMEN

1. Control (Wachenfeldt)		
Primigravidas	11,378	
Total	26,481	= 42.9%
2. Tuberculosis (our series)		
Primigravidas	18	
Total	51	= 35.3%

COMPLICATIONS

The complications which occurred were mostly tuberculous in nature or caused by tuberculosis: Secondary anemia (4), tuberculous laryngitis (2), Pott's disease (1), tuberculous cervical adenopathy (1), and tuberculous meningitis (1). Some were obstetric in nature: Toxemia (2), pernicious vomiting of pregnancy (1), and positive blood culture postpartum (1). Finally, two developed psychosis and one pyelonephritis. Five had positive tests for syphilis, a finding which is not surprising considering the large number of colored patients in the series.

TREATMENT

The principle of conservatism is to be stressed. As long as tuberculosis is inactive, the patient should be treated expectantly with the best medical and hygienic measures. At the first sign of activity, sanatorium treatment or its equivalent is imperative. In this connection, it is interesting that one sanatorium near Dresden, Germany, has a separate division for tuberculous pregnant women. A few years ago, Alice Hill surveyed the sanatorium facilities for pregnant tuberculous women in this country. She found them entirely inadequate, in fact they were worse for pregnant women than for tuberculous women who were not pregnant. It appears that the situation has since undergone some improvement. The time when obstetric interference is indicated in active tuberculosis must always remain a matter of individual judgment; the life of the child must be considered as seriously as the life of the mother. Most cases can probably be carried to term and then delivered, if necessary, by cesarean section and then sterilized. When patients go downhill rapidly, it must be determined to what extent this may happen independent of the pregnancy. In hopeless cases, the life of the mother should be prolonged, if possible, in the interests of the child.

The follow-up of our patients included the results from the following questionnaire, personally conducted by the Social Service Department of the St. Louis Maternity Hospital.

1. Is the mother living or dead?
2. Has she sought any medical attention since that delivery? If so, what for and where?
3. Has she had any symptoms such as: (a) cough, (b) fever, (c) loss of weight, (d) night sweats, since the delivery in question?
4. Has the mother been pregnant again since the delivery in question? What was the termination of each delivery? What is the *condition* of the children resulting from these pregnancies?
5. What is the *condition* of the children resulting from the pregnancy in question?

TABLE VII. FOLLOW-UP SERIES

	Living	33	Total Traced	NUMBER OF	
				YES	NO
1. Mothers	Dead	1	34		
2. Subsequent Medical Attention				29	5
Periodic chest examination				11	
Pneumothorax Clinic				4	
Obstetric Clinic				8	
Tuberculosis Clinic				3	
Gynecology Clinic				3	
Mental Asylum				1	
Unclassified				3	
3. Incidence of Symptoms					
Subsequent to Delivery:					
Cough			5		
Fever			2		
Loss of weight			4	5	29
Night sweats			1		
4. Fate of Children					
Normal			24		
Stillborn			4		
Abortion			2		
Delicate			3		
Died at 8 mo.			1		
5. Subsequent Pregnancies:					
Normal infants			6	8	26
Abortions			2		

CONCLUSIONS

This series of 51 cases is too small to permit of definite conclusions. It has been compiled to contribute toward such an accumulation of data as may permit of conclusions being drawn. While it is possible that pregnancy may activate a resting lesion, there is no other evidence that the course of the disease is adversely affected thereby, nor is there any evidence that tuberculosis, except in its febrile stages, adversely affects pregnancy if the case is properly handled. The chief difficulty in compiling such a series lies in the evaluation of diagnostic findings. If the criteria are too strict, many cases will be missed; if they are not strict enough, too many tuberculous cases will be admitted.

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DISCUSSION

DR. JOHN ALEXANDER, ANN ARBOR, MICH.—A crucial point in the discussion of this interesting subject is, in my opinion, whether the pregnant patient has active or inactive tuberculosis. Inactive tuberculosis is frequently diagnosed as "tuberculosis" and, quite obviously, persons with old, inactive tuberculosis may proceed to term with reasonable safety. In the category of active tuberculosis there is almost every degree of activity. (Patients with mildly active fibroid tuberculosis run relatively little risk from pregnancy, provided the tuberculosis is expertly managed both during pregnancy and after delivery. On the other hand, patients with the unstable, partially exudative type of tuberculous lesion are exposed to a very considerable risk of serious progression of their tuberculosis if their pregnancy is allowed to proceed to term.) We have recently had at the University Hospital, among 100 tuberculous patients, two who died of tuberculosis following delivery, and another whose tuberculosis became activated following delivery, although her disease had been brought to a quiescent state by collapse therapy shortly before she became pregnant. When faced with the problem of a patient who has become pregnant in the presence of active tuberculosis, I feel we should ask ourselves the question, If this woman were not pregnant would we permit her to become so at this time? If the answer is in the negative, and if the pregnancy is less than four months old, I believe the patient should be aborted and the tuberculosis actively treated in a sanatorium. After the tuberculosis has been arrested for two, three, or more years (depending upon the case), consideration should be given to permitting the patient to become pregnant with the reasonable expectation that she could then bear a healthy child without risk to her own health and life, and that she might care for the child without exposing it to a great risk of tuberculosis infection and death. Royston and Jensen's data show that only 3 of their 51 patients had cavitation, only 13 had tubercle bacilli in the sputum, and 19 had hemoptysis; it is likely that most of the patients with cavitation and tubercle bacilli are included among the 19 who had hemoptysis. From the data presented I doubt if more than half of the 51 patients, namely 26 patients, had active tuberculosis. If this is true, then 7 out of a possible 26 patients with active tuberculosis became worse or died of tuberculosis during or after pregnancy which, I submit, expresses a very considerable risk. In conclusion, I believe that patients found to have active tuberculosis during the early period of pregnancy should be seriously considered for therapeutic abortion.

DR. G. D. ROYSTON, ST. LOUIS, MO. (closing).—The outcome in a given case depends almost solely upon the period of the infection. Barnes and Barnes found that the pneumococcus type of lesion was present in over 60 per cent of their cases. In the case that has liquefaction and cavity formation, the mortality is higher. The report of Barnes and Barnes, Garshell, Ornstein and Kovnat has shown that pregnancy has little effect upon tuberculosis, although the favorable cases improve at the onset of pregnancy, and the active cases get worse even though the uterus is not emptied. We must add that adverse domestic and financial factors react unfavorably upon tuberculosis. The demands of the children in the house keep the mother from getting proper rest.

We must remember that if the pregnancy is to be interrupted, better results are obtained if this is done early. In former years I was a very active advocate of the teaching that therapeutic abortion should be done for tuberculosis. Today I have reversed myself because if tuberculosis is treated as tuberculosis, the patient may be permitted to go to term.

THE TREATMENT OF CERVICOVAGINITIS IN CHILDREN WITH SILVER PICRATE SUPPOSITORIES*

A PRELIMINARY REPORT

ALFRED J. KOBAK, M.S., M.D., AND LESTER E. FRANKENTHAL, JR., M.D.,
F.A.C.S., CHICAGO, ILL.

(From the Mandel Clinic of the Michael Reese Hospital)

THE treatment of cervicovaginitis as recorded in the literature of the past decade has been subjected to frequent changes. A lack of uniformity of treatment is evidenced, in the literature of any short period, by the variety of therapy advocated. The following methods of treatment have been used (some with good and others with indifferent results): Mercurochrome, silver nitrate, acriflavine, vaccines, diathermy, copper ionization, antiseptic irrigations, and lately the popular usage of estrogenic hormones. The frequent variation of therapy by the investigators treating this clinical entity is an indication that no one has found consistent success with any single form of treatment.

Cervicovaginitis may be divided into two distinct types: (1) Specific or gonorrheal, which in general is the more severe and more difficult to cure; and (2) the nonspecific, which has been found to have less severe symptoms and is caused by a variety of organisms, and is frequently more amenable to therapy. Both forms of vaginitis are characterized by a vaginal discharge, which may vary in its intensity. Examination shows localized evidences of inflammation by the presence of a discharge ranging from slight to profuse in amount and from serous to mucopurulent in consistency with a tendency to crust when it dries on the skin. The vestibule and vulva have an irritated appearance. The vagina and cervix are likewise affected in varying degrees of intensity. Beyond these local findings, one rarely observes any systemic or generalized complications. Many of these children are undernourished and may have some degree of secondary anemia. This ailment is found most frequently in the poorer classes where hygiene is bad.

The management of these patients has two objects. First, and most frequently stressed, is the local treatment to eradicate the causative organisms; and second, the improvement of local hygiene by cleanliness, and the general health by a well-balanced diet with addition of vitamin therapy whenever possible.

*Read at the Eighth Annual Meeting of the Central Association of Obstetricians and Gynecologists, Detroit, Mich., October 15-17, 1936.

The vaginitis clinic of the Michael Reese Hospital was established by Irving Stein, who personally supervised it up to seven years ago. The treatment advocated by him and his associates¹ consisted of daily injections of 1 per cent mercurochrome 220, incorporated in hydrous wool fat mixed with an equal amount of petrolatum. The mixture was first warmed to render it soft, and then injected at room temperature, high into the vagina. The mothers were instructed how to do this, and when necessary, nurses made visits to supervise and personally treat the child. Stein found results of this treatment to be very satisfactory. These procedures were continued by us for four years but it was felt, despite the good results obtained, that there was room for some improvement. Primarily, we noticed that the ointment rapidly oozed out and stained the garments of the child, which mothers reported to be objectionable. The efficacy of this treatment was therefore felt to be impaired by the rapid loss of much of the material injected. An attempt was made to study other methods of therapy and possibly find one that would insure easier application. A form of medication was desired that the mothers could easily apply by themselves, and one that would find its way into all the crypts of the vaginal canal and still not be expelled prematurely with subsequent loss in its efficiency. The latter was our experience with all ointments. A silver pierate suppository was adopted because it answered these objections and has been tried for one year. Our results with its usage are the basis of this preliminary report.

METHOD OF TREATMENT

The patients were examined at each visit with the infant vaginoscope, and thereby, the condition of the cervix and vagina was observed and progress notes made. By means of this instrument, a smear was taken from the vaginal portion of the cervix. When insufficient material was obtained from this source, smears were also taken from the vagina. The mother of the patient was instructed to cleanse the vulva between the labial folds daily or more often with a soft cloth, and to use bland soaps such as castile or super-fatted types. The insertion of the suppository was demonstrated to the mother at the child's first visit. She was instructed to keep the suppository in the refrigerator to maintain its maximum rigidity and for lubrication to use only cold water. During the hot weather, an instrument was devised to facilitate in the introduction of the suppositories. A supply of suppositories was furnished with further instructions to inject every night before bedtime so that the chance of its premature expulsion would be minimized. This treatment was to be omitted the night before the next visit to the clinic. The mothers were likewise instructed as to diet whenever the child appeared undernourished. Many of our patients are under the care of the department of pediatrics.

At each visit a record was taken of the mother's statement as to the progress made and she was asked whether there was any discharge from the standpoint of the child's clothes being soiled by contact with the genitals. Daily treatment was administered by the mother until the discharge and signs of inflammation disappeared, and the smears became negative. Then the treatment was gradually spread out until the patient was receiving no local treatment and merely returned for purposes of smear examinations. The patient was considered cured when the discharge, local

findings, and the smears were all negative for three successive months. However, the children were observed for longer periods whenever possible.

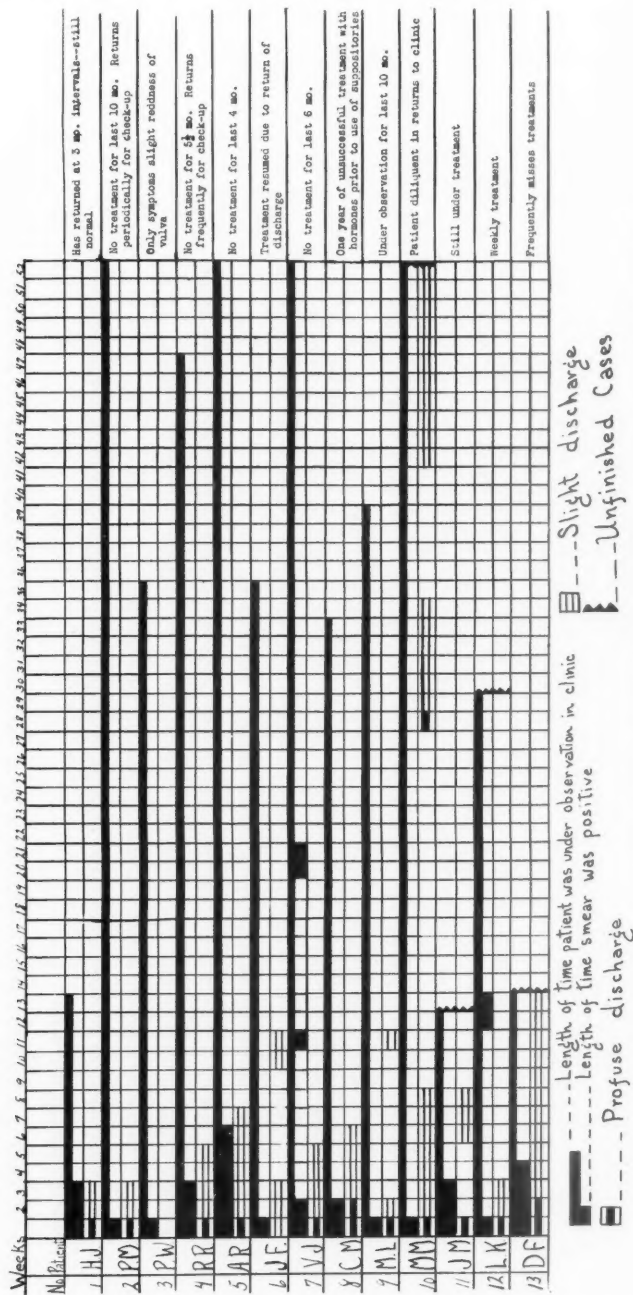


Fig. 1.—Results in the treatment of patients that had smears positive for the gonococcus.

The results of this form of treatment, as shown in Figs. 1 and 2, are self-explanatory. The patients showed rapid and definite improvement as evidenced by the quick disappearance of the discharge. The recorded observations of the mothers also

confirmed this improvement. Five of the patients had a permanent negative smear after one week of treatment, and three became negative in three weeks. Four patients became permanently negative after six to nine visits to the clinic. Only one patient remained resistant to treatment and did not become permanently negative until fifteen clinic visits had been made. The nonspecific group likewise showed a rapid response to this therapy.

DISCUSSION

The treatment with silver picrate as outlined was easy for the mothers' use. The group of patients treated in our series consisted of seven negroes and fifteen whites. We felt that the cooperation of the class of mothers we were dealing with could be assured only when their duties

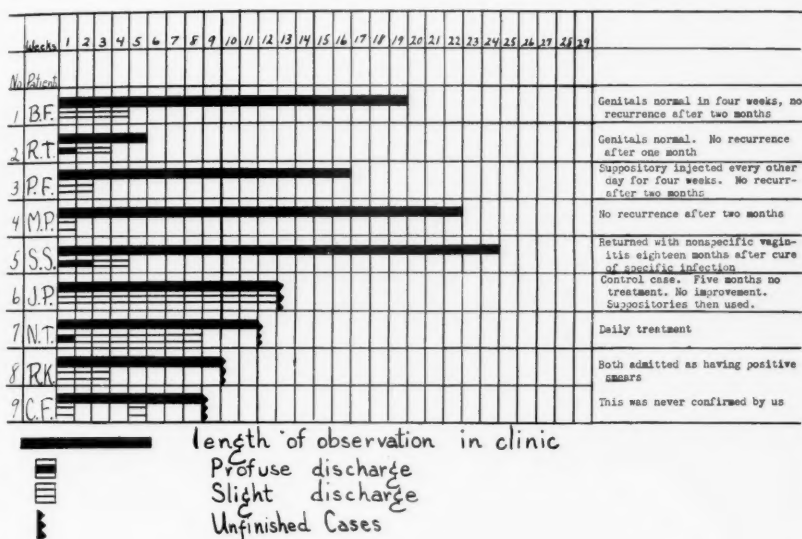


Fig. 2.—Results in treatment of nonspecific vaginitis.

were easy to comprehend and did not entail too much effort. Before starting to use the silver picrate suppository, we had also tried neisogel injections, and estrogenic hormone. Both methods of therapy proved unsuccessful in our hands. The hormone injections, besides being expensive and painful to the child, have not given the satisfactory results claimed by others. Witherspoon² and Schauffler³ were not encouraged by their results with hormone therapy. TeLinde and Brawner⁴ observed very good results following the use of estrogenic hormone in the vaginal suppository form. Here the rationale of this treatment was ease of administration. The effect was indirect, i.e., after the systemic absorption the action of the hormone is referred back to the vaginal mucosa to bring about its beneficial changes. It is hard to conceive that local benefits of hormone can be better achieved this way than by direct systemic intro-

duction (intramuscular), unless there is a beneficial effect of the basic content of the suppository which in TeLinde's series was glycerin and carbolic acid.

The more rational treatment is one that aims at the immediate etiologic agent by direct application of an antiseptic substance on the diseased tissue, and the indirect treatment by improvement of the local hygiene and general health of the child. Schauffler very aptly stated, "The time-worn theory that the infantile canal is carpeted by a thin, weakly resistant mucous membrane is untenable, as proved by repeated gross and microscopic examinations. In the infant and small child, the vaginal canal constitutes an ideal 'harbor of infection,' whereas in the adult it does not. Obvious characteristics of the immature vagina account for the mechanical retention of organisms and for changes in the secretions favorable to their existence. These are (1) hymenal occlusion (relative); and (2) the contracted cryptiform accordion-like conformation." The illustrations of this contributor well support his contentions. The suppository adopted and used in our series was of such size that it should readily pass the hymen, and of such length that it occupied the entire length of the vagina. It has a boroglycerin gelatin base. The dosage of silver picrate was 1 gr. to each suppository. It melted readily at body temperature and appeared to diffuse easily throughout the surface of the vagina into its crypts. The material was observed to adhere well to the vaginal surface with which it came in contact. The series of cases that make up this report, is not very large. Four additional patients in whom we were obtaining good results, did not return to complete the treatment. In view of the encouraging results obtained in this small series in so short a period of time, we will continue to study this treatment.

SUMMARY AND CONCLUSIONS

Twenty-two patients with cervicovaginitis were treated with silver picrate. Thirteen were found to have positive smears for gonococcus. The results obtained were considered very encouraging.

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DISCUSSION

DR. HARRY M. NELSON, DETROIT, MICH.—Cervicovaginitis in children is primarily a public health or clinic problem. The average gynecologist sees none or perhaps very few cases, and the pediatrician does not treat many. Therefore, we must depend for most of our knowledge of this condition on our public health clinics.

In 1935 the Social Hygiene Division of the Detroit Board of Health treated 97 cases of gonorrheal vaginitis in children, by instillations of 10 per cent protargol solution in glycerin, given weekly. The mother was instructed to irrigate the

child at home twice daily, with a weak solution of potassium permanganate. This was done over a period of four weeks when smears were taken. If five successive smears were negative the patient was said to be cured. The average length of treatment for all ages was 103.5 days, for those under five years, 132 days, and for school children 89 days.

The sources of infection may be of interest. There was a positive source discovered in 60, or 66.6 per cent. In 54 per cent sources were found in the home; in 6.6 per cent the origin was a sexual contact; 5.5 per cent were said to be contracted cases; 4.4 per cent of the cases were contracted in hospital nurseries.

Our method of hormone therapy has been to give 100 rat units of theelin each day for a week, then three times a week until negative smears are obtained. In the majority of cases we obtain negative smears in four to six weeks. This treatment seems to cut down the duration of the disease though we do not know what effect it may have on the child in the future or what effect it may have on the ovaries.

DR. IRVING F. STEIN, CHICAGO.—Some years ago I found at Michael Reese Hospital that some cases of vaginitis in children came to the pediatricians, a few to the gynecologists, a few to urologists, and no one group agreed on a uniform plan of treatment. We suggested that the three departments come together, but after we had organized a special clinic, pediatrics and urology dropped out of the picture and left the problem to me entirely. Since then I have been able to maintain interest in the subject in the Gynecological Department.

In the literature there is great enthusiasm expressed in favor of hormone treatment, but my own experience with it was discouraging. I want to commend the routine use of the vaginoscope in examination. I have never seen any harm come from its use, and have never had to stretch or cut the hymen in order to insert the instrument. I get a great deal of helpful information from its use in cervicovaginitis.

DR. H. C. HESSELTINE, CHICAGO.—The use of the vaginoscope has been justly stressed. I would like to emphasize again its value in diagnosing the occasional case of a foreign body. The diet, particularly with regard to the vitamins, is most important.

Have any of these patients had reactions? This question is raised as I have been reliably informed that an occasional adult may have such a reaction. If this reaction is the result of ionization with formation of picric acid, then perhaps there is less likelihood of such in the child because of the comparatively low acidity, even alkalinity of the vaginal moisture.

Were there any cervical infections, and if so, what other therapy than suppositories did you use? How many of the gonorrheal patients had anal infections, and how were these infections treated?

DR. KOBAK (closing).—The change in the content of the smears is one way of observing the progress the patient is making. In the beginning we find the smears to be full of leucocytes and these contain morphologic forms of gonococci. As the patient improves there will be a disappearance of the gonococci but the pus cells predominate. With continued improvement epithelial cells are seen in increasing numbers, and as they do so the pus cells become progressively diminished in numbers. In the cured case we see nothing but the epithelial cells and occasional bacteria.

When we first began to use the silver picrate suppository we were uncertain when to advise the mothers to discontinue the injection of the suppository. Our experience soon taught us to advise the treatment daily until all signs of inflammation had vanished, the discharge reported absent by the mother, and the smears negative. Then we instruct the mothers to increase the intervals between the injections and,

if findings continue to remain negative, we eventually have the patient returning to our clinic, although she has had no suppository injections at all. Thus many of our patients are seen at two- and three-month intervals merely for observation.

Our standard of cure is three consecutive monthly smears that are negative, together with absence of all other findings. We try to have our patients come as long as possible to check against any possible recurrence.

Our results with estrogenic hormone have been disappointing. We have had six patients under this form of treatment and gave them as much as 2,000 units a day. After long periods of time our patients were still uncured by accepted standards. One patient had a positive smear after eleven months of treatment with associated profuse discharge and local findings of acute vaginitis. When we transferred this patient to the present form of treatment the smear became permanently negative in one week and the discharge disappeared shortly thereafter. We followed this patient for ten months and never noted any recurrence.

After one year's usage of this suppository treatment we have felt very much encouraged by the good results that practically always followed. We have had no anal infections. We had one case of bartholinitis before we tried this form of treatment. We had none of the adult complications, but we did find cervical lesions. There were small erosions and the portio vaginalis often appeared injected. To make these observations we depended upon the vaginoscope. Without its use we could never see what changes were occurring above the hymen, and thus have a direct check on the progress the patient was making during the course of treatments.

MATERNAL MORBIDITY*

SIX YEARS STUDY OF 4,837 CASES AT THE EVANSTON HOSPITAL

ROBERT M. GRIER, M.D., EVANSTON, ILL.

(From the Department of Gynecology and Obstetrics of Northwestern University Medical School and of the Evanston Hospital)

IN THIS report is presented a study of morbidity occurring in the cases delivered in the Maternity of the Evanston Hospital beginning in 1930 and continuing through 1935. In these six years 4,837 women were delivered of 4,885 viable babies. There were 5 deaths, a mortality rate of 0.10 per cent. There was only one death from puerperal infection. The American College of Surgeons standard for morbidity has been used. Any woman whose temperature rises to 100.4° F. on any two or more days, not including the day of delivery, has been considered morbid. Temperatures have not been taken every four hours. A morning and evening reading only is taken as a routine. If fever appears, the temperature is taken every four hours until normal. According to Stander bidaily temperature readings instead of four-hour readings reduce the incidence of morbidity to one-third.

Including cesarean sections the gross figure of morbidity was 6.5 per cent. When these are excluded the incidence was 5.0 per cent. It will be seen therefore that this operative procedure increased the incidence by about 30 per cent.

*Read at the Eighth Annual Meeting of the Central Association of Obstetricians and Gynecologists, Detroit, Mich., October 15-17, 1936.

The ratio of morbidity according to the type of delivery has been analyzed and is shown in Table I.

TABLE I. RATIO OF MORBIDITY, 1930-1935

TYPE OF DELIVERY	BABIES DELIVERED	% INCIDENCE OF METHOD	% MORBID	RATIO
Spontaneous	2,267	46.4	3.8	1
Low forceps	1,994	40.7	5.0	1- 1.3
Breech extractions	158	3.4	7.6	1- 2.0
Midforceps	165	3.2	13.3	1- 3.5
Podalic versions	80	1.6	16.2	1- 4.2
Cesarean section	221	4.5	38.5	1-10.1
Total	4,885	99.8+	6.5	1- 1.7

If the incidence of morbidity for the spontaneous deliveries is taken as a basic figure, 3.8 per cent, and if we call this one, we can forecast the increased risk of morbidity for the other types of delivery. A chart indicating the increase of morbidity for the various obstetric operations has been posted in our delivery rooms as a warning to us all. Next to cesarean section, midforceps and version and extractions carry the highest incidence, 13.3 per cent and 16.2 per cent, respectively. The frequency as compared with spontaneous deliveries is 3.5 to 1 and 4.2 to 1. Thus it is shown that the more radical the procedure the greater the risk of morbidity.

Version and extraction was done in only 1.6 per cent of our cases. Midforceps deliveries were done in 3.2 per cent, the incidence being less than that of cesarean section, which was 4.5 per cent. We hope to reduce the frequency of abdominal delivery, as its morbidity rate is 38.5 per cent or ten times that of spontaneous delivery. In a former report the author showed the high incidence of fetal mortality for version and extraction. This same group of operators promptly reduced the incidence by about one-half to its present low level. When one realizes the dangers of a procedure it is usually avoided far more than would be thought possible.

Other factors influence morbidity beyond question. Some of these will be shown. It is generally agreed that puerperal infection may arise from foci of infection elsewhere in the body. This can be controlled partially by the elimination of such foci early in pregnancy. We all strive to do this with our private patients as well as with clinic patients. Infection was shown by Semmelweis and Holmes to be carried to patients by the physician through the lack of asepsis. Eradicating this faulty technic was a great step forward. Now perhaps we are too complacent with our "good" aseptic technic. I think that our record is not good and not bad, but can be improved. By reducing our operative procedures to a minimum, especially those that show a high rate of morbidity, we believe we can reduce our figure considerably. Our incidence of operative deliveries is high if outlet forceps

are included. It will be seen, however, that the morbidity of this procedure differs but little from that of spontaneous delivery, namely from 3.8 per cent to 5.2 per cent.

Parity alone appeared to influence morbidity very little. In the 4,837 women in this report 48 per cent were primiparas and 52 per cent were multiparas. In the 319 morbid patients this proportion was about the same, 46 per cent were primiparas and 54 per cent were multiparas.

Other obstetric maneuvers and accidents are found to contribute to morbidity. We have studied some of these, such as cervical tears, induction of labor, spontaneous or artificial rupture of the bag of waters and uterine packing. Table II shows that the risk of morbidity is definitely increased when a cervical tear is produced. Perhaps the slight increase for breech extraction is due to the smallness of this series. In the entire series, however, the increase is 120 per cent.

TABLE II. MORBIDITY AND CERVICAL TEARS, 1930-1935

TYPE OF DELIVERY	NUMBER DELIV- ERIES	NUMBER TEARS	% TEARS	% MOR- BID GEN- ERAL	NUM- BER MORBID WITH TEARS	% MORBID WITH TEARS	% INCREASE MOR- BIDITY OVER GENERAL
Spontaneous	2,267	109	4.8	3.8	7	6.4	60
Breech extraction	158	17	10.7	7.6	1	8.3	9
Low forceps	1,994	158	7.9	5.2	22	12.7	154
Midforceps	165	38	23.0	13.3	9	23.6	77
Podalic version	80	9	11.2	16.2	3	33.3	105
Total	4,664	331	7.9	5.0	42	12.4	120

Induction of labor was studied only for the past four years during which time accurate figures have been kept. The usual procedure for the induction of labor is a modified Watson method. Some men have employed a warm soapsuds enema instead of the castor oil. As a rule we do not attempt induction of labor unless there is some effacement and dilatation of the cervix. The colpeurynter was used sparingly, nine times, and then only for placenta previa or severe toxemia in multiparas. There were 292 inductions in 2,045 deliveries or 9.5 per cent. Twenty of these were morbid, an incidence of 6.8 per cent which is practically the figure for the entire group. In our experience medical induction does not increase morbidity.

Among the patients who were morbid there was almost an equal number with membranes ruptured spontaneously or artificially and this corresponds with the experience in all the deliveries. The average time from rupture of the membranes to delivery in the cases in which spontaneous rupture occurred was 11.4 hours. In the cases in which the membranes were ruptured artificially, it was 2.3 hours. In this

series then we can say that very little effect was noticed in the morbidity rate for spontaneous or artificial rupture of the membranes.

Uterine packing was employed quite freely when indicated. We believe that anemia or loss of blood increases the risk of infection very materially, and such has been the common experience of most obstetricians. Thus, we do not wait until a great deal of blood is lost before packing the uterus with from 5 to 10 yards of gauze, but resort to this procedure whenever the uterus tends not to stay contracted. It was used in 2.1 per cent of our cases (Table III). It is more widely

TABLE III. MORBIDITY FOR UTERINE PACKING, 1932-1935

TYPE OF DELIVERY	NUMBER PACKED	% PACKED	% PACKED MORBID	% MORBID GENERAL	% INCREASE MORBIDITY OVER GENERAL
Spontaneous	17	1.3	5.8	3.8	52
Low forceps	24	1.6	29.1	5.0	480
Breech extraction	7	6.2	0	7.6	0
Midforceps	8	10.3	0	13.3	0
Podalic version	7	14.0	28.5	16.2	75
Total	63	2.1	15.8	5.0	216

used after the difficult operative maneuvers or prolonged labor. The morbidity rate was thus naturally high, 15.8 per cent, for all uterine packings. It is hard to say what the rate would have been had the patient been allowed to bleed more extensively.

The technic in the delivery rooms has been essentially the same with but few exceptions. The use of rectal examinations has been employed as a routine. However, vaginal examinations are done occasionally if deemed necessary. Most of the time during the past few years 4 per cent mercurochrome has been injected into the vagina prior to a vaginal examination and the doctor always puts on a sterile gown and gloves. The patient has a complete perineal preparation. In the last three years sodium pentobarbital and scopolamine have been used in 62 per cent of our cases during labor. This has been mentioned as a factor likely to increase morbidity. Except for the first year of its use when there was a sharp increase, our morbidity has been getting less than before. Table IV shows these yearly comparisons.

TABLE IV

	BEFORE USE OF NEMBUTAL			AFTER USE OF NEMBUTAL		
	1930	1931	1932	1933	1934	1935
Per cent morbid	7.7	6.9	6.5	8.3	5.7	4.4
Per cent three-year averages			7.0			6.1

Artificial rupture of the bag of waters has been done in approximately half of the cases. In the morbid cases this was practically the same ratio. Frequent use is made of episiotomy, in primiparas 86 per

cent and multiparas 53 per cent. Induction of labor is not too widely used but withal sufficiently often, 9.5 per cent. The method used has been described.

The vaginal and perineal preparation solutions used have been green soap and mercurochrome, acetone, and alcohol. Since November of 1935 for economical reasons, we have been preparing a compound colored alcoholic solution of mercuric chloride for skin disinfection. This was described by Vaichulis and Arnold from the Department of Bacteriology and Public Health of the University of Illinois. It can be prepared for \$1.60 per gallon. So far we have not noticed an increase in infections, and are satisfied with its use.

The personnel of the delivery rooms has been the same as far as nursing supervisors are concerned for far longer than the six years included in this report. There is a training school for nurses in the Evanston Hospital and each pupil nurse receives six weeks of obstetric training in the delivery rooms.

There were three internes on the obstetric service for three months at a time, each constantly on duty in the maternity for a shift of at least eight hours a day. They assisted with all deliveries. For the past three years, most of the time, we have had a clinical clerk, a fourth-year student from Northwestern University Medical School, who assisted with all deliveries. They remained with us on twenty-four-hour duty for six weeks.

TABLE V. PERSONNEL

DISTRIBUTION OF DELIVERIES	NUMBER DELIVERIES	PER CENT OF DELIVERIES
Staff	2,992	62.0
Internes (clinic)	618	12.8
Courtesy obstetricians	621	12.8
General practitioners	606	12.4
Total	4,837	100.0

To Dr. William C. Danforth, who has been the Chief of the Department of Obstetrics and Gynecology for the past fifteen years, goes much of the credit or responsibility for this record. He has established its technic and policies. He has trained, to a great extent, all of the three other members of the staff. The work distribution is, I think, unique for a general hospital (Table V). Most of the women, 62 per cent, were delivered by the staff. In addition 12.8 per cent were clinic patients who were delivered mostly by the internes, but always under the direct personal supervision of one of the staff. Another 12.8 per cent were delivered by six nonstaff obstetricians who are trained men and limit their practices to obstetrics and gynecology. Only 12.5 per cent were delivered by 44 different men in general practice. Practically all of the latter men confine their obstetrics to the simpler procedures and call consultation freely when complications are feared.

This being one of the requisites of the courtesy privileges extended to them. This control of the work and the continuance of the same trained personnel and essentially the same birth room technic, which was familiar to all, was one of the principal reasons for these results. A careful detailed tabulation of all work is kept day by day so that from month to month and year to year results are known and can be studied. Any man who does not do continually good work is removed from working privileges or reprimanded. Any procedure showing unsatisfactory results was done as little as possible or eliminated.

An analysis of the different diagnoses given for the 319 morbid patients was made. It is not essentially different from those in other reports, but is given here as a matter of record. Sixty of these women, or 18.8 per cent, had some fever on admission. Puerperal infection, including metritis, endometritis, parametritis, peritonitis, pelvic cellulitis, phlebitis, and puerperal infections, accounted for 75.2 per cent of the morbid (Table VI). Mastitis was the cause of fever in 8.7 per cent of our cases, being next to the puerperal group in frequency.

TABLE VI. CAUSES OF MORBIDITY

TYPE OF DELIVERY	NO. MORBID FOR TYPE	PUER- PERAL IN- FECTION ^a		MASTITIS		PYELITIS		RESPIRA- TORY		EXTRA- NEOUS	
		NO.	%	NO.	%	NO.	%	NO.	%	NO.	%
Spontaneous	87	58	66.1	11	12.6	6	6.9	5	5.7	8	9.1
Low forceps	100	75	75.0	13	13.0	2	2.0	10	10.0	1	1.0
Breech extraction	12	6	50.0	2	16.6	-	-	2	16.6	2	16.6
Podalic version	13	10	76.1	1	7.7	-	-	1	7.7	1	7.7
Midforceps	22	17	77.2	1	4.5	3	13.5	1	4.5	-	-
Cesarean section	85	74	85.8	-	-	2	2.3	5	7.5	4	4.6
Total	319	240	75.2	28	8.7	13	4.0	24	7.5	16	4.9

Respiratory infections accounted for 7.5 per cent. These included ordinary colds, laryngitis, bronchitis, bronchopneumonia, lobar pneumonia, and pulmonary tuberculosis. In 4.0 per cent of the febrile cases pyelitis was found. All the others, or the fevers from extraneous causes, amounted to 4.9 per cent. In this latter group are included two cases of acute endocarditis both of whom died, with positive blood cultures of hemolytic *Streptococcus viridans*.

In conclusion, this study, we think, has shown us that morbidity can be reduced.

1. Reduction to a minimum of the more radical types of delivery such as, midforceps, high forceps, version and extraction, and cesarean section is most essential.

2. The number of cervical tears should be reduced as much as possible by conservative obstetrics and the avoidance of the more extensive forms of intervention.

3. Uterine packing carries a high rate of morbidity but should not be delayed too long as the hemorrhage is equally dangerous.

4. Maintenance of good delivery room technique is very important. This can best be maintained by an unchanging nursing staff.

5. Excellent obstetrics may be done in a general hospital where the majority of the work is done by a well-controlled group of trained obstetricians.

6. An analysis of work, for which good records are essential, tabulated monthly and yearly is all-important in preventing laxity and is a stimulus to better work.

DISCUSSION

DR. WINTON T. STACY, St. JOSEPH, Mo.—Any statistical study that is done of work in a hospital tends to improve that work. This report of 5 to 7 per cent gross morbidity is about the average morbidity one will get in looking over well-regulated institutions. If you get a rise in morbidity, look to your work. This report emphasizes (1) conservative obstetrics, (2) the necessity of an organized, well-trained obstetric nursing staff, (3) the supervision of courtesy obstetricians and general practitioners, and (4) a standard of morbidity.

The standard of morbidity used here made no mention of a rise of temperature after the tenth day postpartum nor inclusion of fatal cases. Bidaily readings were recorded. Some of us believe that if readings are made every four hours we would get an increased morbidity. It is interesting to note that 19 per cent of the patients had fever on admission. Temperature is a symptom. Many men have advanced the theory that we should base our morbidity records not only on temperature rise, but upon any evidence of definite or prolonged pathologic condition with or without fever, resulting from childbirth, because definite pathology has been found in patients whose temperatures never reached 100.4° F. Almost every childbirth leaves a little damage, therefore accepting this standard of morbidity we would get a direct proportion to parity. Using rise of temperature as an index for morbidity this is not true, as shown by the essayists. Perhaps we use temperature readings because two or more can read a thermometer alike, whereas it is often difficult for two, equally competent men, to agree upon a diagnosis of a pelvic inflammatory condition.

The relation of the seasons of the year to morbidity was not discussed. Some increase in morbidity, due to upper respiratory tract infections, may be expected during the winter months. I do believe we have more unaccountable temperature elevations during the hot summer months. During the past summer in a study of morbidity I attributed it to the external temperature, 110 to 112° F.

Morbidity may be the first step toward mortality. Dr. Grier has brought out the fact very clearly that morbidity is directly proportional to the severity of the operative procedure, and has worked out a ratio chart that would be well to have in every obstetric ward. In this respect his findings are similar to those of other writers, but do not agree with those who find a direct proportion between (1) length of labor, (2) rupture of membranes, (3) vaginal or rectal examinations and morbidity.

This paper, through and through, is an argument for conservative obstetrics with minimal interference, and then only when indicated. It is proof of the fact that excellent obstetrics may be done in a general hospital where properly trained men supervise the work of those doing obstetrics, calling attention to their results by means of tabulation of the work done.

We should adopt a standard of morbidity. As yet, we must accept an elevation of temperature to 100.4° F. on two consecutive days not including the day of delivery nor after the tenth postpartum day. The method of taking temperature is of little importance.

DR. IRVING F. STEIN, CHICAGO.—I would like to emphasize what Dr. Grier brought out and what Dr. Stacy seconded, that the amount of kind of interference is a most important factor in producing morbidity. I would like to emphasize one other point, namely, that antiseptics play a very minor rôle in prophylaxis. At Michael Reese Hospital a number of years we have used various external antiseptics, starting with bichloride external douche over the perineum, in the preparation, and the use of bichloride solutions for frequent rinsing of the gloves, during delivery. Then we used lysol, and later we painted the perineum with one-half strength iodine. Then mercurochrome was tried. Even antedating the Mayes' technique, we used external but not internal mercurochrome antiseptics in obstetric preparation. Then after a few years we decided that sterile water was just as good if our technique was improved. We compared a given number of cases prepared with sterile water taken at random from our records with an equal number in which the agent of preparation was mercurochrome, iodine, and later merthiolate, using Mayes' technic for the latter, and we found the morbidity in each series about the same percentage. We do not feel that antiseptics play any important rôle. In consequence we have eliminated even the hand basins containing antiseptics that we used for rinsing gloves and use sterile water instead, and our morbidity has shown no increase over the years in which we did use the various antiseptic agents.

I would like to bring out one other point, that after two serious accidents with bichloride solution in the hospital in our department, we have persuaded the general staff and the administration of the hospital to eliminate bichloride of mercury from the hospital. At the present time with a wide selection of antiseptics which are adequate for thermometer sterilization, and other instrument sterilization that formerly called for bichloride, we believe that bichloride should be eliminated from hospital routine and available only if ordered specifically from the drug room by a given physician. I think that is a distinct step forward in teaching asepsis, and in eliminating these unfortunate accidents which occasionally were encountered.

DR. GRIER (closing).—Of the five deaths we had in this series the causes of death and the types of delivery were as follows: (1) Puerperal infection following spontaneous delivery. (2) Acute endocarditis following spontaneous delivery. (3) Acute endocarditis following cesarean section. (4) Postpartum hemorrhage following cesarean section. (5) Lobar pneumonia; patient was delivered at home and brought to the hospital immediately following delivery.

We do not believe that antiseptics play a great part in morbidity, consequently we are using the solution mentioned which can be made as cheaply as possible, namely \$1.60 a gallon. We think that morbidity can be reduced and the following conditions are of great assistance: (1) A well-controlled staff of trained men. (2) Proper delivery room supervision and careful maintenance of technique, and, (3), avoiding the more radical types of delivery. I think the figures in this report indicate this. We are also convinced that a study of this kind has helped us. In checking up on our results we will find when to reduce this morbidity. In a previous report, we have found that our fetal mortality following version and extraction was entirely too high, consequently delivery by this method has been reduced 50 per cent.

LYMPHANGIOMA OF THE OVARY*

R. S. SIDDALL, M.D., AND W. R. CLINTON, M.D., DETROIT, MICH.

(From the Department of Obstetrics and Gynecology and the Department of Surgery, Harper Hospital)

TRUE lymphangioma seems to be among the rarest of the tumors arising in ovarian tissue. In fact, until 1908 the existence of such a growth was doubted. In that year Kroemer reported two authentic cases. In a search through the literature we have found the report of one other tumor which was probably of this type, although the author (Fleischer) believed it to be lymphocystic degeneration of the ovary. Rössle reported a lymphangioma found in the ovary of a ten-month-old child, which, however, had developed from subcutaneous tissue in a dermoid cyst. Schottländer's third case was probably also of this kind, and therefore not a tumor originating in true ovarian tissue. The tumor reported below we believe to be a true lymphangioma developing within and from the ovary.

CASE REPORT

Negress (Harper Hospital Case No. 122106), forty years old, married for a number of years but never pregnant. She complained of a mass in the abdomen which had been present for two years and had enlarged considerably during that time. There had been progressively developing dull pain which was most marked at time of menstruation. Constipation had been present since the onset of her trouble, and for six months before admission there had been slight swelling of the ankles. The patient also complained of a femoral hernia. The past history was unessential except for the fact that the menstrual periods had been irregular and frequent with intervals of only six days to three weeks. They had also been profuse at times. At the last period, ending one week before admission to the hospital, there had been bleeding for eight or ten days with cessation for one and one-half days and then bleeding again for six days.

Physical examination showed nothing noteworthy except marked obesity, blood pressure of 180 systolic and 100 diastolic, slight edema of the ankles, and a lower abdominal tumor. This tumor could be felt as a firm nodular mass extending up to the level of the umbilicus in the midline and somewhat to the right. It was movable above but was fixed in the pelvis at its lower pole. On the day after admission, operation was performed under novocaine spinal anesthesia. Supravaginal hysteromyomectomy, bilateral salpingo-ovariectomy, appendectomy, and bilateral femoral herniorrhaphy from within the peritoneal cavity were done. The postoperative course was febrile from the second to the sixth day with the highest temperature 102° F., but was otherwise uneventful.

The specimen consisted of the uterus (amputated supracervically), fallopian tubes, ovaries, and the appendix. The uterus measured 18 by 13 by 10.5 cm. due to many fibromyomas of which one at the fundus was the size of an orange and another

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smaller one just above the point of amputation measured 4 by 4 by 3 cm. Both tubes appeared normal, and the right ovary showed nothing of note except several small cysts. The left ovary was of special interest. It was pear-shaped, measuring 8 by 7 by 5 cm., and was somewhat uneven in contour but not definitely nodular. The consistency suggested a solid tumor, but there was not the degree of firmness as is found with such tumors as fibromas. Cut section showed a uniform, light colored, and well-defined solid tumor occupying all of the mass except for a crescent-shaped and compressed layer of ovarian tissue fitting like a cap over one end. This ovarian tissue contained several small cysts.

Microscopic examination, except for the findings in the left ovary, was of little interest. The largest fibroid showed areas of hyaline degeneration, and rather sparsely glandular endometrium was in an early proliferative phase. Cysts of the right ovary were of the simple follicle type. Both tubes and the appendix were normal.

Sections from different parts of the tumor in the left ovary showed essentially the same picture throughout, the structure consisting largely of spaces lined by a single layer of endothelium and varying in size from that of small capillaries up to eight to ten times their diameter. A few spaces contained coagulated material in which were occasional small or large round cells. The spaces were obviously lymph vessels. The endothelium showed no buds or other evidence of proliferative activity. In some parts of the tumor the lymph vessels lay directly against each other, but usually there was a layer of connective tissue between. This stroma or framework was usually very thin, and nowhere was it broader than the width of the medium-sized lymph spaces. It was composed of connective tissue of a loose fibrillar and sparsely cellular type with the cell nuclei rather large and round, or spindle-shaped. There were no areas of extensive or advanced degeneration in the tumor, though the endothelium of a few vessels showed pyknotic or faintly staining nuclei. Also, the stroma in numerous, but scattered and small, areas between the lymph spaces had undergone hyaline degeneration with disappearance of nuclei. These changes were more common in the deeper portions of the tumor. Nowhere was there obliteration of the lymph vessels, mass necrosis, or cyst formation.

The tumor was surrounded for most of its circumference by a thin capsule of fibrillar connective tissue resembling that found between the lymph vessels and in which there were similar though larger areas of hyaline degeneration. The fibrils lay parallel to the surface of the tumor, and from them the connective tissue framework of the tumor proper seemed to originate. Over a small part of the periphery the capsule thinned away and finally seemed to disappear so that the lymph vessel development was covered by the germinal epithelium only. In the capsule there were a moderate number of rather large lymph vessels and also a few small blood vessels and capillaries. In the tumor proper was seen only one small area with blood vessels. This was just beneath the capsule, and there were only a few, scattered, blood-filled capillaries lying among the lymph spaces. Elsewhere in the tumor all the spaces were obviously lymph vessels. There was a small round cell or lymphocytic infiltration throughout the connective tissue framework and capsule. In the latter were seen several small collections of lymphoid cells resembling tiny lymph nodules.

At one pole of the tumor was the thin crescent of ovarian tissue with the points extending about one-third around the periphery. Here was found normal appearing ovarian tissue, mainly the cortical type. There were several developing follicles and two structures resembling small follicular cysts, in one of which was fresh (traumatic?) blood. The tumor was stripped away from the normal appearing ovarian tissue for the most part, but where still attached its capsule showed a transition or merging of tissue and cell type into that of the denser and more cellular ovarian cortex.

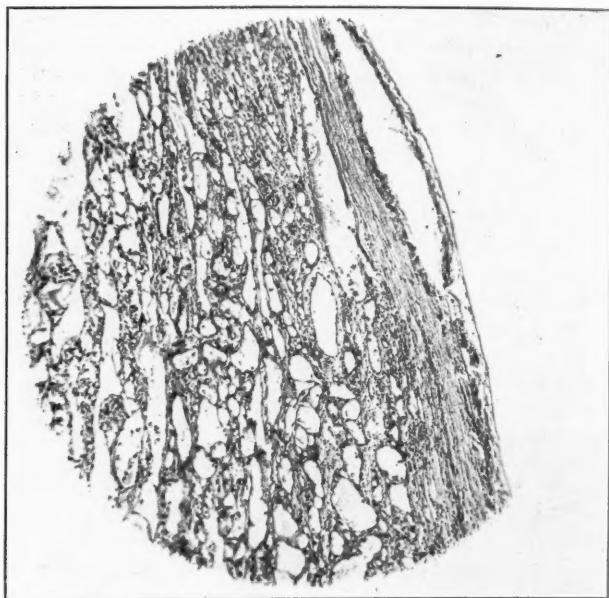


Fig. 1.—Lymphangioma of the ovary. Low power showing the lymph spaces and also the connective tissue capsule of the tumor.

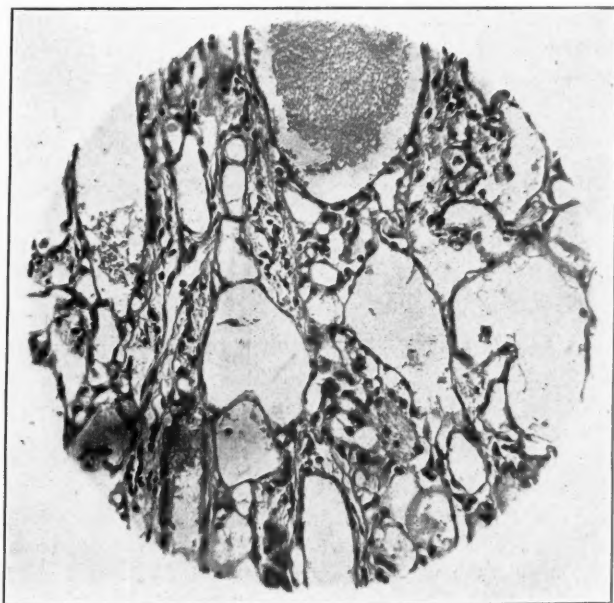


Fig. 2.—Lymphangioma of the ovary. High power showing the endothelial-lined lymph spaces.

Pathologic Diagnosis.—(1) Cavernous lymphangioma of the ovary. (2) Fibromyomas of the uterus, hyaline degeneration. (3) Follicle cysts of the ovary. (4) Normal fallopian tubes and appendix.

COMMENT

Histologically, our tumor agrees very closely in every respect with those described by Kroemer, except in one particular. His tumors were both large (the largest being twice the size of a child's head) and doubtless because of their size had undergone advanced necrosis and cystic degeneration in their central parts. This was apparently similar to the frequent finding in the deeper portions of large lymphangiomas from other parts of the body. Fleischer's tumor was somewhat smaller than ours, measuring 7 by 5.5 by 5 cm. The endothelial-lined spaces varied in size from that of a pinhead to a lentil. There was no evidence of degeneration except for a loss of endothelium in some of the spaces. He preferred the diagnosis of lymphocystic degeneration rather than lymphangioma, chiefly because there were no suggestions of active endothelial proliferation such as are found in lymphangiomas of the lip, tongue, and cheek. Evidences of rapid endothelial growth were likewise lacking in our tumor, but the picture was definitely that of an enlarging though circumscribed and benign neoplasm. Kroemer evidently considered his tumors to be newgrowths and was careful to differentiate them from lymphangiectasis. He even questioned their essential benignity as will be mentioned later.

The infrequency of lymphangiomas of the ovary is established so far as published reports are concerned. However, Kroemer doubted their extreme rarity and expressed the belief that many had been overlooked because of the lack of a distinctive gross appearance. Yet, in the twenty-eight years since his report it would seem that a number of these tumors, if they are not actually highly infrequent, would have been found by chance and been reported. Meigs states that he has never seen one in the pathologic material from the Massachusetts General Hospital, and our case is the first to be found during the last five years at Harper Hospital among approximately two thousand microscopically examined ovaries.

Because of its apparent infrequency, lymphangioma of the ovary is at present of little importance clinically. For the same reason, its prognosis in respect to recurrence has not been determined though pathologically our tumor appears to be benign and examination of the patient twenty-two months after operation showed no return of the growth. Unfortunately, our patient did not return for observation after discharge from the hospital. Kroemer was unable to follow his patients, and Fleischer gave no subsequent history for his case. Kroemer considered his tumors to be potentially malignant because of a third growth found in an ovary next to an atretic follicle. This

was also a lymph vessel tumor, but here was a structure suggesting sarcoma. Both the endothelium and the stroma cells were undergoing active proliferation and had become round cell in type. The endothelial lining of the larger lymph spaces was reduplicated to form a many-celled layer. He suggested the possible progression of a lymphangioma to such a picture or even to that of malignant endothelioma.

We wish to thank Dr. Plinn F. Morse for his kind assistance and permission to use this material from the laboratory.

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DELIVERY FOLLOWING STILLBIRTH FROM DYSTOCIA IN
PREVIOUS PREGNANCIES*

ARTHUR B. HUNT, M.D., AND ROBERT D. MUSSEY, M.D.,
ROCHESTER, MINN.

(From the Section on Obstetrics and Gynecology, the Mayo Clinic)

THE obstetric patient who becomes pregnant after having lost her first baby from dystocia presents a problem of more than ordinary interest. Her case represents a challenge to the attending physician to obtain a live and healthy baby with a minimum of risk to the mother. Often the history of the first delivery, which resulted in death of the fetus, may be incomplete or vague, and the physician must supplement such information with careful objective findings during pregnancy and at term to decide on the best method of conducting labor. In spite of this, however, plans for delivery frequently must be revised, without much notice, at term or after the patient is in labor.

Because a review of the literature (of the last twenty years) has failed to reveal a specific reference to cases of this interesting group, we feel our rather small series of cases merits report. We wish to present a series of 33 consecutive patients who in the last ten years came to the Section of Obstetrics at the Mayo Clinic with the history of having lost their first baby in labor or shortly thereafter as a direct result of some form of dystocia. There were 38 stillbirths among these 33 patients, as 5 patients had each had 2 stillbirths before coming to the clinic. None of these 33 patients was therefore the mother of a live baby. Dystocia is here interpreted in its broad sense as any difficult labor or delivery,

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not only from actual bony disproportion between the fetal head and maternal pelvis, but also from other causes, such as malfunction of the pelvic soft parts or anomalies in presentation of the fetus.

In all but a few cases the fetus was at or near full term and was of sufficient weight and maturity to withstand at least the rigors of an average labor and delivery. In the few cases in which the fetus was not so sturdy because of prematurity, actual cephalopelvic disproportion existed.

ANALYSIS OF PREVIOUS DELIVERIES

Nine of the 33 patients had been delivered as primiparas at the clinic; the remainder had been delivered elsewhere. The 5 patients who had had stillbirths twice had likewise been delivered elsewhere. The average length of labor for 18 of these 33 women had been thirty-two hours and twenty minutes, although a third of these primiparas had labored sixteen hours or less. The average age at the time of previous delivery was twenty-six years and two months, or about the average for primiparous women seen at the clinic. Four of the patients in the series were less than twenty years of age, 5 more than thirty, at the time of the previous delivery. The oldest was thirty-seven years old; therefore, the elderly primigravida was not frequently seen in this series.

An analysis as to the cause of the first stillbirth in some of the cases cannot be entirely accurate, owing in some instances to the difficulty of obtaining an accurate history of what transpired at the first delivery; in most cases, however, the cause of previous stillbirth could be rather readily determined.

Operative delivery with its frequently accompanying trauma had been necessary in 22 cases. Bony disproportion was estimated in these cases to have been present in 16 instances. Dystocia resulting from the dysfunction in the pelvic soft parts had been encountered in at least 5 instances and probably more. Breech presentation had been recorded in 6 instances, about 6 times the normal incidence, which is usually given as approximately 3+ per cent. There was one face presentation.

While no searching inquiry as to the employment of pituitary extract in labor was made, its injudicious use in 2 cases probably explained the fetal deaths. The history was especially clear in 1 case. There was also 1 instance of prolapsed cord associated with a contracted pelvis.

The data as to the method of the previous delivery were not available in 4 cases. In 12 cases delivery was referred to as "instrumental," usually implying forceps delivery. Six patients had been delivered by breech extraction, in 3 cases forceps having been applied to the after-coming head. A clear history of 3 midforceps and 2 high-forceps deliveries was given, and 2 craniotomies had been performed after a high-forceps operation had failed. One fetus was stillborn by cesarean section after a high-forceps delivery had failed.

According to the histories, the incidence of immediate maternal morbidity was not great. Three patients, however, had a history of having been febrile and confined to bed for a month or more. Later morbidity was evidenced in 8 cases by the extensive vaginal and perineal scars. There was one third-degree laceration and one rectovaginal fistula.

An inquiry into the incidence and type of pelvic contraction is pertinent. Seventeen of the 33 patients in the series had definite pelvic contraction, general contraction in 7 cases, funnel in 4, flat in 3, and in the remaining 3 unspecified. Four additional patients apparently had normal pelves, but there must have been a serious dystocia as evidenced by the history and subsequently by failure of the test of labor. In 1 case dystocia was due to a definitely oversized fetus. In 4 cases the live baby which was delivered subsequently through the pelvis was of greater weight than the stillborn fetus of the first pregnancy; 3 of these subsequent deliveries were spontaneous, 1 was a midforceps delivery.

One may conclude, we believe, that in these cases either soft tissue dystocia or premature operative interference was the cause of stillbirth at the first delivery. As further evidence of this, 10 of these patients were later delivered of their infants through the pelvis with relative ease.

DELIVERIES AFTER PREVIOUS STILLBIRTH

The method of delivery to be employed for parous women whose babies have previously been born dead makes an interesting study. As term approaches a selection must be made of those patients for whom a test of labor may be tried. The fact that a woman has lost a baby from dystocia does not indicate, per se, that elective cesarean section must be employed routinely in subsequent deliveries.

The following analysis of deliveries subsequent to labor resulting in stillbirth will show that often no single criterion will decide which cases are suitable for the test of labor. Disproportion is the most important single factor. Twelve patients in the series were not allowed a test of labor but were submitted to elective cesarean section. Nine of these 12 had contracted pelves, and in most instances the head could not be depressed to the ischial spines. The average weight of the fetus was 8 pounds (3.6 kg.). In the 3 remaining cases without pelvic contraction, placenta previa was present in 1, a second patient had already had 2 previous stillbirths, and in the third case the head of a very large baby was unengaged as labor began.

The remaining 21 patients in the series were allowed a test of labor. Seventeen of them were delivered through the pelvis, with 1 fetal death. In the 4 remaining cases, in which the test of labor failed, the patients were delivered by cesarean section. There was, therefore, only 1 stillbirth in this group of cases, and this delivery was classed in the group in which the test of labor failed because the baby was lost. The test of

labor was accordingly successful in 16 of the 21 cases or 76.2 per cent. There was no maternal mortality in this group.

The most complete report of the results of trial of labor to come to our attention is that of Bailey and Williamson. They reviewed 676 cases in which patients in labor had contracted pelvis and observed that 90.1 per cent delivered through the pelvis with a maternal mortality of 0.44 per cent and a gross fetal mortality of 6.2 per cent. We feel that our results of the test of labor compare favorably with this experience when one considers that all of our patients had previously had stillborn infants from dystocia.

As has been said, 5 patients had previously had 2 stillbirths each. One of these patients with a normal pelvis was successful in subsequent test of labor and delivered from below spontaneously; all of the others were treated by cesarean section, one after an unsuccessful test of labor. The pelvis of 2 of these 4 were normal, of the other 2, contracted.

In 3 of the 6 cases of original breech presentation, there was a recurrence of breech presentation. One patient was delivered successfully (breech presentation), one was submitted to cesarean section, and the third delivered spontaneously after external version. The treatment of these 3 patients illustrates the value of modifying treatment to suit the case by careful individualization.

In 2 cases of contracted pelvis a small live baby was very easily delivered when a large baby had been lost from dystocia in the first pregnancy. These patients will probably be what Solomons calls "dangerous multiparas" in future pregnancies. In addition there were 5 other patients for whom skepticism might be entertained as to their obstetric future. If, then, to these 7 are added the 16 who underwent cesarean section, there are 23 who might be classified as "potentially dangerous multiparas," leaving only 10 (30 per cent) for whom normal delivery might be expected in the future.

Many patients returned for a third or fourth delivery, there being 17 additional deliveries of this type. In these cases the conduct of the second delivery seemed to determine the outcome in subsequent deliveries: Patients who were formerly successful in the test continued to deliver successfully through the pelvis, and those who had to submit to cesarean section were all treated by abdominal delivery.

RESULTS

There were 88 deliveries in this series of 33 patients. Two babies were lost in deliveries subsequent to initial stillbirths (Table I), in one case stillbirth being due to dystocia and in the other the infant dying on the eighteenth day after cesarean section from congenital anomaly complicated by urinary infection. The pathologic diagnosis in this latter case was: congenital dilatation of the bladder and multiple abscesses of the kidneys.

TABLE I. FETAL MORTALITY

	LIVING	DEAD	PER CENT MORTALITY
First delivery (at clinic or elsewhere)	0	33	100.0
Second delivery (elsewhere)	0	5	100.0
Second delivery (in five cases the third)	32	1	3.1
Third and subsequent deliveries	16	1	9.3
Total deliveries after first stillbirth	48	2	4.0
Corrected fetal mortality*			2.0

*On basis of 1 fetal death in 50 deliveries subsequent to stillbirth, the other infant dying of a congenital anomaly and urinary infection eighteen days after cesarean section.

In viewing the results, then, of 50 deliveries subsequent to stillbirth from dystocia, there were 2 (4 per cent) fetal deaths, 1 from stillbirth and 1 neonatal death on the eighth day from a congenital anomaly. Deducting this latter death as having no connection with delivery, the corrected fetal mortality is 2 per cent. Since all infants were stillborn in the first delivery, the fetal mortality can be said to have been reduced 98 per cent for the series. In the 88 deliveries, there was 1 maternal death from sepsis on the third postpartum day following elective cesarean section, making a maternal mortality of about 1 per cent. Because of the high incidence of conditions conducive to dystocia (for example, more than half of the patients had contracted pelvis), a somewhat higher maternal mortality might have been expected.

In 10 cases there was puerperal morbidity (a temperature of 100.4°F. on two successive days on any day from the second to the ninth, inclusive); all 10 patients were delivered by cesarean section.

SUMMARY AND COMMENT

Thirty-three patients, all of whom had lost one or more babies in a previous pregnancy from difficult labor and delivery, were delivered at the clinic. In 50 such subsequent deliveries, there were only 2 fetal deaths, 1 a stillbirth and the other from a congenital anomaly, or a corrected mortality of 2 per cent. There was only 1 maternal death from sepsis (1.0 per cent). The maternal morbidity was 20 per cent, and this occurred only in cases in which cesarean section was performed. Following delivery through the pelvis, there was no maternal mortality or febrile morbidity and only one baby was lost.

Three factors producing the dystocia that was present at the first delivery are not usually seen at the time of the second delivery: (1) soft-tissue dystocia, (2) breech and other abnormal presentations, and (3) the injudicious use of pituitrin in the first stage of labor. In certain instances these conditions seemed to explain the stillbirth at the first pregnancy. A test of labor may well be advised in such cases provided there seems to be no cephalopelvic disproportion. The test of labor was successful in 76.2 per cent of the cases in which it was employed. In

the sixteen cases in which the test of labor was successful, the duration of labor averaged eight hours and twenty minutes. The length of trial of labor before failure was evident and cesarean section had to be performed was more than twice this long (sixteen hours and forty-eight minutes). It, therefore, seems that the test of labor should not be too prolonged, especially as a long test increases the maternal, and to some extent the fetal, risk.

Because of the presence of scars from cesarean section, contracted pelvis, or pelvic disproportion, 23 of the 33 women in this series may be considered as "potentially dangerous multiparas."

Prenatal care is of special value in the type of case reviewed. Careful and repeated pelvic measurements may be made. Repeated examination as term approaches gives a fairly accurate idea as to whether or not serious disproportion may exist. A more complete history may be volunteered or obtained. Breech presentations may be turned to cephalic by external version, in some cases to allow a test of labor. Labor may occasionally be induced to advantage before term. The physician should take the time to observe and study each case from all angles, so that he will be thoroughly familiar with its important details when the time for delivery approaches.

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DISCUSSION

DR. JAMES R. GARBER, BIRMINGHAM.—The authors have stressed three important things: prenatal care, the problem of labor, and the possibility of delivery. When a case of pregnancy first comes to the doctor, he is somewhat in the position of an architect, and begins to develop a blueprint by careful prenatal observation. He continues to develop the blueprint until the woman is in labor, at which time he must be governed by that unknown quantity which is uterine behavior. The last thing to be considered is why and when to operate. I believe from a practical viewpoint I would rather know the why and when than the art, though that is, of course, important.

DR. RUDOLPH W. HOLMES, CHICAGO.—In different hospitals the stillbirth and neonatal death rate varies considerably, the average being about 7 per cent, but as many are due to congenital causes as to dystocia. The fact that a woman has a difficult first labor, possibly eventuating in fetal death, does not carry any certainty of dystocia in subsequent labors. The first baby had the problem of dilating the soft parts, which are thus prepared for the egress of later children. Many a time I have had the trying experience of a difficult first labor, and later ones were surprisingly easy, even precipitate. Karl Braun, all of seventy years ago, enunciated his dictum based upon many, many thousands of labors that a woman's first baby is usually large: her second the smallest, and only after she has borne seven children is the birth weight comparable to the first child's. A difficult first labor, with or without stillbirth, entitles the woman to careful observation in her next parturition, but no more or no less than should be accorded a woman who has a diminution of pelvic capacity. A test of labor in an abstract sense should always be granted her

before rushing to a section. In the published report of my 92 cesarean sections, now sixteen years ago, I showed that in my experience the only difference between the results of a primary over a secondary operation is that the former has a more placid postoperative course. Results are determined by errors of omission or commission during the period of the test. For a true test to be given, labor must continue until full dilatation is nearly attained. There should be no vaginal examinations, and rectals should be strictly limited to pressing indications.

DR. HUNT (closing).—The duration of the test of labor depends more on the patient's condition than the actual time, also on the type of pains and whether the membranes have been ruptured or not. The psychic factors in these women were not mentioned, yet they were important, for every woman in this series had lost a baby because of hard labor and came to her second pregnancy with a good deal of dread. Even so, I feel we should give most of these women the test of labor when the case warrants it. We sometimes give the woman's husband warning when about to make a test of labor, and in borderline cases the patient and her husband are given some option in selection of the type of delivery, after the relative risks are discussed. Cesarean section has been avoided where possible because of its higher maternal risk.

Cini, Natale: Experimental Research Upon the Influence of Pregnancy Upon the Development of Tar Carcinoma in White Mice, *Folia gynae.* 33: 273, 1936.

The author states that from the complexity of data, clinical and experimental, it is not clearly understood what influence pregnancy exerts upon the development of malignant growths. With this object in view, the writer undertook the present experimental work upon white mice which had been subjected to carcinoma incited by tar.

The author concludes that pregnancy does not influence proliferative manifestations in the tumors of the white mice, nor does it influence the proliferative manifestations to carcinoma if the lesion was present prior to the pregnancy; but if the pregnancy is superimposed upon simple lesions already undergoing proliferation it facilitates and hastens this process.

The author makes a plea for further research in this problem, which might explain certain apparent contradictions observed in clinical cases.

MARIO A. CASTALLO.

Olsen, A.: Precocious Motherhood, *Acta obst. et gynec. Scandinav.* 16: 121, 1936.

Among 24,000 labor cases at the Jutland Lying-In Hospital there were 269 patients under seventeen years of age at the time of delivery. Of these, 3 were thirteen years old, 8 were fourteen, 42 were fifteen, and 216 were sixteen years old. Complications of pregnancy and labor were less frequent among these young children than among older women. Of these 269 babies 143 were males and 126 females. Two-hundred fifty-three were discharged alive. Among the very young mothers there was a high incidence of cases where the father of the child was an older man or a close relative of the patient. The author is of the firm belief that extreme youth in pregnancy is not a serious complication or a justification for therapeutic abortion.

J. P. GREENHILL.

A TEN-YEAR STATISTICAL REPORT OF CARCINOMAS OF THE CERVIX*

FRANK WARD SMYTHE, M.D., MEMPHIS, TENN.

(From the Gynecological Department of the University of Tennessee)

THIS report is a review of 357 cases of patients with malignant cervixes who were admitted to the Memphis General Hospital from the first of 1926 to the last of 1935. There were 76 white patients and 278 colored ones. This is about the average racial proportion of this Institution's admittances.

Classified anatomically in Group 1 were 16; in Group 2 were 26; in Group 3 were 79; and in Group 4 were 192. In a fifth group there were 26 cases. This group contained those hopeless cases in which there was no chance for any active therapy to aid. In addition to the above 5 groups, the records of 18 cases did not state their classifications.

Cytologically there were only two adenocarcinomas. This is quite a small percentage and may be accounted for by the fact that so many of these cases were in Groups 3 and 4 that, probably, some late cases had lost their tendency to form glands.

The average age was 42.5 years. The oldest patient was eighty-one and the youngest was nineteen years of age. Sixty-six cases occurred after the menopause. There was none before puberty. Of interest were 42 cases in patients twenty-nine years of age and under (14.99 per cent). The average duration of symptoms was six and one-half months, the longest being forty-eight months and the shortest one week. Of these patients 275 had borne children with an average of 4.4 children each. The largest number of children was 23. Twenty-seven (9.63 per cent) had never been pregnant. Sixteen had never borne a child, but had aborted one or more times. Fifty patients (17.85 per cent) had a positive serologic test for syphilis. Five patients certainly had a delivery through a cancerous cervix. One patient was pregnant when the cervical lesion was diagnosed. In 2 cases an additional malignancy was present, one a carcinoma of the breast and the other a sarcoma in the left axillary region. Supravaginal hysterectomy had been done previously in 14 cases. In no case had a chronic cervix received any radical treatment such as surgery, radium, or cauterization.

The active therapy in the first four groups consisted of x-ray and radium. Only 3 patients had operations. Two of these had total

*Read at the Eighth Annual Meeting of the Central Association of Obstetricians and Gynecologists, Detroit, Mich., October 15 to 17, 1936.

hysterectomy following radium, and one had x-ray after a total hysterectomy. Because only 53 per cent of these clinic patients have been traced, the percentage of apparent cures could not be accurate, and is not given.

SUMMARY

From this review of 357 malignancies of the cervix, the following can be deduced:

Periodic examinations must be made. Not only is it necessary for the patient to come to the physician, but he must examine her (and far too often he fails to do this).

The age of patients, after adolescence, apparently has no bearing on the incidence of carcinoma of the cervix except, with everything else being equal, the younger the patient the more rapidly fatal the disease.

Deliveries in this series seem not to have affected the percentage, as 91.37 per cent of patients admitted to the Gynecological Service in this hospital had borne children.

The tragedy of expulsion of a child through an unknown cancerous cervix can be prevented by a careful examination shortly before the expected time of delivery.

When supravaginal hysterectomy is done, the remaining cervix should be given careful attention to insure its reaching a healthy state.

All chronic cervixes should receive proper treatment so as to prevent, as far as possible, their undergoing a malignant change.

The most satisfactory results have been from x-ray and radium therapy.

DISCUSSION

DR. E. F. SCHNEIDERS, MADISON, WIS.—The mental picture of the majority of physicians regarding a case of carcinoma of the cervix is that of a parous woman in the late thirties or forties with a history of atypical bleeding and abnormal discharge. It is therefore of great interest and greater importance to have cited to us the fact that 42 cases of these 357, or 15 per cent, occurred in patients twenty-nine years of age or under, some as young as nineteen years of age. The usual conception has always been that from 95 to 97 per cent of the patients with carcinoma of the cervix had borne children whereas in this series, 27, or approximately 8 per cent, had never been pregnant and 82, or approximately 23 per cent, had never borne a child.

The high incidence of a positive test for syphilis, namely 17.85 per cent, in conjunction with the above cited facts occurring in a series such as this in which cervical infections undoubtedly have been high, lends support to the theory of Beall, Proctor, Regaud, and others that infection and inflammation are more important than lacerations and scars as factors predisposing to the development of cancer in the cervix.

I feel that we should commend Dr. Smythe for having presented to us this rather drab picture of a condition which undoubtedly is paralleled in many of our respective communities. Real tragedy is exemplified in the fact that in only 16 cases of Group 1 and 26 cases in Group 2, a total of only 42 out of 357 cases, or approximately 12 per cent, is there a reasonable expectancy of permanent cure. The vast majority of the remaining 315 were doomed as soon as diagnosed, regardless

of method or procedure. That such is still the usual picture is suggested by the fact that national statistics show that only about 2 per cent of all cases of carcinoma of the cervix are diagnosed while in early clinical Grade 1. Recent detailed study in Massachusetts, New York, and Pennsylvania has brought forth the information that there is an average delay of twelve months between the onset of symptoms and the institution of adequate therapy and that at least 50 per cent of this avoidable delay is the fault of the physician or physicians involved in the case. It is necessary, therefore, that continued effort be put forth by every available means to educate not only the public but our own ranks as well so as to alter the present situation. That such is possible has been proved in Massachusetts where, after an active educational campaign of six years, it was noted that there was an increase of 36 per cent in the cancer population in the general hospitals of the state. This was a 50 per cent greater increase than the increase in other states. Furthermore, there was no yearly increase in the cancer death rate since 1926, the first time in the history of any state that such results had been achieved. Detailed study showed that the improvement in results was found to have occurred in the accessible cancer groups, one of which is cancer of the cervix.

I do not believe that the final salvage of treated cases will be greatly increased by further developments in therapy, but I do feel that the more universal application of the knowledge now available could almost completely reverse the statistics. Furthermore, I firmly believe that in prophylaxis lies a great opportunity for improvement. I mean thereby the thorough eradication of benign cervical pathology by whatever means indicated, be it cauterization, conization, plastics, amputation or complete removal in conjunction with hysterectomy. We undoubtedly all agree in the logic of the above statements but such is not the general practice by the rank and file of the profession who in reality are still caring for the vast majority of women. That such prophylaxis is effective is strongly suggested by the many thousands of cases reported in which follow-up studies over many years have shown a negligible incidence of carcinoma occurring in cervixes so treated. Microscopic study of tissue removed for benign lesions by Pemberton and Smith in a series of 5,960 cases showed 2.39 per cent of cervix cancer and suggests that in many instances thorough treatment of the supposed benign pathology actually cures occasional cases of very early unrecognized cancer. Certainly this may be the case in so-called "cancer in situ."

Of great personal interest is the fact that in a series of 3,500 cases observed personally during the past twelve years following treatment of the benign pathology there has occurred no carcinoma up to the present time. Also, that in no case of carcinoma of the cervix which has come under our care has there been previous treatment of the cervix. Furthermore, the ratio of cancer of the cervix to cancer of the fundus has been completely reversed in our practice, so that for a number of years we actually have seen more cancer of the fundus than cancer of the cervix. Might this not be due to the fact that for years we have been teaching, preaching, and practicing thorough therapy of benign cervical lesions?

DR. J. P. GREENHILL, CHICAGO.—Most of the papers that have appeared in the literature during the last few years concerning carcinoma of the cervix have dealt, as the one we have just heard, with treatment and results. Notwithstanding the advances made in therapy during the last few years, we have salvaged at most about 25 per cent of the patients. In other words, at least three out of four women with carcinoma of the cervix die of the disease. As the last speaker said, our chief hope lies in prophylaxis and education of the laity and physicians. I arose only to make a plea for the 75 or 80 per cent of women who will eventually die of carcinoma of the cervix. These women sooner or later develop constant excruciating pain. Heretofore we have given these women increasing doses of codeine and morphine. A few years ago I urged the operation known as pelvic sympathectomy

for relief of pain associated with carcinoma of the cervix. We soon found that if we operated on all the women with carcinoma of the cervix we relieved only 50 per cent of them. However, if we performed the operation on women who have pain in the lower abdomen, in the back, the rectum, the bladder, or pain associated with rectovaginal and vesicovaginal fistulas, we can relieve almost 100 per cent. Later we resorted to injections of 95 per cent alcohol in the subarachnoid space, and we are pleased to say that in a series of more than 100 cases we are relieving about 85 per cent of these women regardless of the location of the pain. There is one type of pain which cannot be relieved by alcohol injection or by sympathectomy, and this is the pain due to obstruction of the ureter, with resulting hydronephrosis and hydro-ureter. This pain can only be relieved by elimination of renal function either by nephrectomy or by irradiation of the kidney. Practically all other types of pain associated with carcinoma of the cervix can be relieved almost entirely by the injection of alcohol into the spinal column. The technic is simple and every woman who has carcinoma of the cervix and suffers severe pain should have the benefits of this simple injection.

DR. W. H. VOGT, ST. LOUIS, MO.—I think a paper of this sort is always valuable to a general society particularly, rather than to a gynecologic society. The incidence of cancer is apparently on the increase. Whether there is a real increase or not or whether the apparent increase is due to the fact that we are making the diagnosis earlier, I do not know. At any rate, if we are going to get anywhere with the treatment of carcinoma, we must see the patients early in order to treat them satisfactorily, and to do this we must educate the general practitioner. In the past few years I have been interested in the work of the American Association for the Control of Cancer and have been giving talks throughout the states of Illinois and Missouri. I have been impressed with the lack of knowledge among practitioners in general regarding carcinoma.

There is another thing that the essayist brought out in his paper, that is the occurrence of carcinoma in early life. Too many people still think that carcinoma is a disease of advanced years. In the admissions at the hospital of St. Louis University since April, 1935, of 75 patients with carcinoma of the cervix, we have up to the present date eleven cases of cervix cancer in women ranging from twenty-one to twenty-nine years of age, and all of these with the exception of one were in Group 2 or 3; only one was a Group 1 case. When we see general practitioners treating cases of bleeding and calling it the menopause, where are we going to get in preaching these things in gynecologic meetings? Get the message to the general practitioner that carcinoma is a disease occurring at any time of life. When a woman comes to you who has been under the care of a general practitioner for thirteen months, bleeding steadily and no pelvic examination made, there is need for more education of the general man.

DR. QUITMAN U. NEWELL, ST. LOUIS, MO.—In 1926 we organized our cancer clinic at Barnes Hospital in St. Louis and have reported our cancer work from time to time, and we have accomplished considerably more in the handling of these far-advanced cases than one would suppose. I do not believe, because a case is far advanced, in Group 3 or 4, that the patient is going to die. Some of them show response to treatment much better than the earlier ones. I believe all patients should be treated just as rigidly, whether they be early or late. In our clinic we treat cervical carcinomas by radium and x-rays and only occasionally we perform a complete hysterectomy and that is on the very early cases. Our statistics show we operate upon less than 5 per cent of the patients applying for treatment. We have a five-year cure of 23.9 per cent.

In the past few years our efforts have been directed toward cancer prevention. We are attempting to educate both the physician and lay public in regard to cancer.

We must educate the patient to see her family physician at least once each year, and then the physician must make a careful examination of the patient and correct any pathology of the cervix he may find. In this way we will have many less cases of cervical cancer applying for treatment.

DR. E. F. SCHNEIDERS, MADISON, WIS.—In a period of twelve years' time in 3,500 personally conducted cases in which we have cleaned up the cervix thoroughly either by cauterization, conization, plastic, or amputation, we have yet to find the first case that has developed carcinoma. The astounding fact is that in three private hospitals serving the metropolitan area of Madison and surrounding territory, around 75,000 to 80,000 people, that the relationship between carcinoma of the cervix and carcinoma of the fundus has been completely reversed. We are seeing each year fewer cases of carcinoma of the cervix. Dr. Vogt mentioned that carcinoma of the cervix is on the increase. In our particular area it is on the decrease. We are seeing more cases of carcinoma of the fundus than carcinoma of the cervix. I am hoping that it is due to the fact that for many years the profession has been teaching and preaching the necessity of complete and thorough cleaning up of these benign cervical lesions. I am reporting this at this time because we are making a study of a larger area to see if this is merely a coincidence or whether there is something to it.

DR. SMYTHE (closing).—Relative to the question of Dr. Newell, since establishing our clinic, our results, not only in gynecologic patients but in patients with carcinoma of other organs, are definitely better. I agree with him that in these groups where active therapy can be practiced that we should not deprive the patient of a chance to get well. In Group 4 we have a patient cured for seven years and two for over eight years.

Dr. Vogt called our attention to a very important thing which I mentioned in only a sentence in this paper, relative to professional education. I have long since stopped talking cancer to men who have been practicing ten years. I think if we are going to get anywhere as far as our medical knowledge is concerned, we have to get the doctors while they are internes and residents, and get nurses while in training. It is a waste of time to talk to a man practicing ten years who is not cancer wise.

I believe that carcinoma of the cervix particularly is on the increase. Probably it is due to the increase in average longevity of the individual, because the older the patients in the group the more malignancies we have. A relative age incidence of forty-two was mentioned in this particular hospital. I was interested that one doctor mentioned a patient eleven years of age. In this regard, there are cases of cancer in patients six months and seven months old mentioned in European clinics.

Dr. Greenhill brought out a very important point relative to the relief of pain in these cases. I have not tried sympathectomy myself. I have tried removing the hypogastric plexus but have had no success. With alcohol injections merely using 7½ per cent absolute alcohol in distilled water, we have had nine cases of malignancy of the cervix, six of which were hopeless. Four died and three of them had malignant ulcers of the rectum. In eight we had relief of pain. Only two had to have slight sedatives, barbiturates. It does not make any difference whether they form a habit or not because they are hopeless.

I appreciate what Dr. Schneiders said about the percentage of positive Wassermanns in the white and colored. I am sorry I am unable to give him any figures. From this study on which this report is made, I feel that almost all had definitely chronic infection of the cervix. The symptoms, I feel, have been longer in duration on the average than the records show. I am sure the symptoms have been present for over six and one-half months.

Department of Practical Problems in Obstetrics and Gynecology

CONDUCTED BY WILLIAM J. DIECKMANN, M.D.

THE DIAGNOSIS OF THE SEX OF THE HUMAN FETUS IN UTERO

STUART B. BLAKELY, M.D., BINGHAMTON, N. Y.

THE problem of the diagnosis of fetal sex has always challenged attention, intrigued interest and baffled solution. Among peoples of all ages and areas, effort has been made in vain to bridge that tantalizingly narrow gap between the observer and the child in its mother's womb. A classification of the means and methods that have been employed in fetal sex diagnosis and a discussion of them in some detail, in each group passing from the "superstitions" to the most recent investigations, is the purpose of this paper. A review, however, is subject to limitations.

While the logic of primitive and less remote thought is often vulnerable, it is not inferior to much current today. Regarding the diagnosis of fetal sex, one might fancy that it proceeded somewhat as follows, but not, however, as a line of conscious reasoning. Marked changes from the normal state are evident in the pregnant woman. These changes must be due to the action or influence of the growing product of her conception. These changes vary in different women and in the same woman in different pregnancies. Some of these variations must be due to some difference in the fetus. The only constant obvious difference in the newborn is sex which must also exist before birth. This difference, i.e. sex, must be the cause of at least some of these variations. The male is profoundly different from the female and is considered to be of greater value, strength, and importance. The effect of a male fetus on the mother must be different in kind as well as greater. Therefore the signs and symptoms of a male pregnancy must differ in character and degree from those of a female pregnancy.

The belief that the pregnant woman betrays the sex of her unborn child, especially if male, is very old. With some exceptions, one can only speculate why and when certain of the signs and symptoms observed in pregnancy were singled out and ascribed to the influence of fetal sex. It is tempting to believe that serology and endocrinology were here in the making, an idea not to be followed too far. From the moment that mankind began to fix time, there gradually gathered about the subject a mass of belief, often strangely in agreement in widely separated parts of the world and in widely varying grades of civilization. Many of these ideas and beliefs, popular in origin and frequently hoary with age, were appropriated, rationalized and elaborated by

ancient and medieval medicine. With the rise and growth of new ideas in anatomy and physiology in the sixteenth and seventeenth centuries they were largely dropped by the science of the day, to revert to and to become again, for varying periods and in varying forms and degree, the property of folk belief on the subject. Through the years these colorful ancient concepts have gradually faded in the West until among us today, in marked contrast with other obstetric superstitions, only the faintest traces exist. Until shortly after the middle of the last century nothing of scientific value or resulting from scientific effort (as we understand science) was added toward the solution of the problem. But those old folk beliefs, call them superstitions if one will, about the means and the possibility of foretelling the sex of the unborn child must not be unceremoniously cast aside. They are worthy of study and of more than a tolerant or amused interest. Age-old wisdom merits respect.

All means that have *ever* been used to diagnose fetal sex may be placed in two great classes: supernatural and natural.

The means employed in the first class were the prophetic interpretation of numerology (still existing as late as the sixteenth century in countries as far apart as China and Italy), astrology and dreams; of the examination of the entrails of sacrificed animals and of the flight of birds; of "ordeals"; of chance happenings and occasions; and of magic formulas and other procedures. Material on this phase of the subject can be found in the first volume of Ploss-Bartels. It is interesting that the use of strictly supernatural means to diagnose fetal sex was never persistent or extensive, compared with the second class. I have not met nor heard of a survivor. Legendre records a French folk belief in a curious mixture of lunar influence and numerology.

The second class, comprising the natural means to diagnose fetal sex, from time out of mind to the very present, may be divided into three broad groups.

Group 1. The supposed origin of the male from the right side of the uterus, the female from the left; and the changes in the right side of the pregnant woman's body ascribed to, or imagined to result from, such origin.

Group 2. The position, outlines, attitude and activities of the fetus during pregnancy and labor.

Group 3. The effects of a male fetus on the total maternal organism; i.e. the reactions of the female body to the introduction therein of a male element. This is the largest and most important group.

GROUP 1

A notion of antiquity was that the human uterus consists of right and left cavities, as is normal in many animals which were the chief source of the ancients' ideas of anatomy. Since the right side has always been considered the stronger, superior and "holier" side and the male the stronger, superior and more valuable sex even in its mother's womb, it followed that the male must develop in the right side of the uterus, the female in the left. Hippocrates taught that "The male fetus is usually seated in the right, the female in the left side of the uterus." After it was known that the human uterus is not normally duplex, the idea became current that the male came from the right ovary, the female from the left. This must have been, however, a comparatively recent develop-

ment, for knowledge of the part played by the ovary and the ova in reproduction is not old. Through historic time this idea is found scattered from China to Europe; right-handed signs and symptoms point to a male pregnancy. There is more pain or heaviness or more or earlier movement in, or more prominence of, the woman's right side, if pregnant with a male. The right breast is larger with earlier milk secretion; the right areola is broader and darker with redder, more injected and more projecting nipple. The right eye is brighter, "softer" and more sparkling with wider pupil. All blood vessels on the right side of the body are fuller and beat more forcibly (the sublingual being especially mentioned), and the right pulse is stronger. The right shoulder is lower, and the right thigh thicker. The woman starts off first with her right foot, and supports herself more with the right hand. Salt does not melt on the right nipple, and the right nostril tends to bleed. Many, if not all, of these may be found in the "*De Secretis Mulierum*", a book ascribed to Albertus Magnus (1193-1280), which was widely used in the scholastic time of medieval medicine.

While right-sided signs and symptoms are no longer valued in fetal sex diagnosis, a bit of the old belief still lingers in the theory of the ovarian or ovular determination of sex. The idea that sex is determined by the egg still lives and will not die, and among men of scientific training. As a matter of fact, the last word on the subject has not been spoken. Otto Schoener published his theory in 1909 and his results in 1924 and 1925. It has given rise to a large volume of German literature. Schoener held, and still holds, that the right and left ovaries alternate continuously in their activities (an idea suggested by Bischoff in 1844); that the human ovum possesses its sex "*Anlage*" before fertilization; and that the sex "*Anlage*" changes, possibly better said, appears, in each ovary in the following sequence: right ovary, male; left ovary, female; right ovary, male; left ovary, female; right ovary, female; left ovary, male. The cycle is repeated *ad infinitum*. E. Rumley Dawson proposed the hypothesis that male and female determining ova are discharged from the ovaries alternately, male from the right and female from the left. Both these men claim that, after the first pregnancy, it is possible to quite accurately foretell the sex of future children by a careful history of the menses (actual and missed), assisted by the palpation of an enlarged tender ovary due to the presence of the corpus luteum of pregnancy. The difficulties of these theories are quite apparent; e.g., menstruation is not always associated with ovulation nor vice versa, and the sex of children after unilateral oophorectomy does not always conform to the rules. Through many years of observing pregnant women, I have never been able to determine any right-sided signs or symptoms peculiar to a male pregnancy, nor evidence of either definitely alternating ovarian activity or of the ovular determination of sex. It is probably safe to deny their existence, though dogmatic statements about the physiology of sex are dangerous.

GROUP 2

The position, outlines, attitude and activities of the fetus during pregnancy and labor.

Hippocrates held that the boy moves in the womb at three months, the girl at four. This idea, with variations in the actual number of the months, was once widespread. It was also thought that

labor was slower with a female child. These conceits are entirely consistent with the belief in male superiority. The girl was supposed to be born "face-up," looking at the rib whence she came; the boy, "face-down," looking at the earth whence *he* came, a bit of Genesis or reminiscent of the usual position at coitus.

In this group belong two modern "natural" means that have been employed in the effort to solve the problem: the x-ray (two procedures) and the rate of the fetal heart. Roentgenologists agree that the ossification of the skeleton of the female is more advanced than that of the male throughout intrauterine life; it has been suggested that this fact might be utilized to foretell fetal sex. Visualization of the fetus in utero (including the outlines of the soft parts), by rendering the amniotic fluid opaque through the injection of strontium iodide into the amniotic sac, occasionally permits the diagnosis of fetal sex, if a true lateral view of the breech is obtained (menees).

In 1859, on the basis of a study of one hundred cases, Frankenhaeuser suggested that fetal sex might be determined by the rate of the fetal heart in the last three months of pregnancy, a persistently slow rate (averaging 124 or less a minute) indicating a boy, and a persistently more rapid rate (averaging 144 or more a minute) a girl. A large number of observations have been made with a corresponding literature. If the male fetal heart is slower, it must be due to some peculiar influence of male sex itself, maleness per se, for which I know of no evidence; or because the male is heavier or bulkier, but the average difference in the birth weights of the sexes would seem to be too slight to have much effect; or the result of some hormonal action, as yet unknown. It is generally conceded today that the method is of no, or at least of very little value, if for no other reason than that the usual fetal heart rate falls between the figures given and so into the uncertain class. Many of the laity express a wistful faith in it. Some physicians, for unworthy or obscure reasons, encourage this faith by professing, at least not denying, the same. Nevertheless, it may lay claim to have been a really intelligent effort to solve the problem.

GROUP 3

The effects of the male fetus on the total maternal organism, cells and organs, their functions and secretions.

In pregnancy, mother and child are a biologic unit. If the mother's own hormones produce well-recognized phenomena, why may not added fetal hormones (which she surely receives) alter these phenomena in degree or character? If the male fetus introduces into her economy new or "foreign" hormones, why may these not alter her response; and, if harmful (as we know they may be), why may they not meet hormonal or humoral resistance (protective)? The maternal response to pregnancy may be physical, or biochemical (using the term in a broad sense), or both. Her reactions may be quantitative, or qualitative, or both. A discussion of these two possible types of reaction now follows.

Aristotle held that, since the female is on a lower developmental plane, a female pregnancy has less effect and makes less demand on the maternal organism than does a male pregnancy; that there is greater body warmth in a male pregnancy and therefore a better circulation; and that on these as a basis the diagnosis of fetal sex is possible. Some observers today agree with Aristotle that a male pregnancy makes

greater demands on the pregnant woman. There is claimed to be more iron in the male placenta; more adrenalin in male urine, and therefore (?) more in the urine of a woman pregnant with a male child. It is said that midwives in the Philippines used to prophesy the sex of the unborn child by the reaction of the pupil of a male dog's eye into which had been dropped some of the pregnant woman's urine. Thinking along this line, I observed the pupillary reaction of twenty-five pregnant women on whom the Bercovitz test of pregnancy was done, to see if the contraction or dilatation of the pupil bore any relationship to the sex of the fetus. The results were negative.

The second idea, that the reaction of the pregnant woman to a male fetus is *qualitatively* different than to a female fetus, is very old, runs as a common thread through most of the ancient methods of sex diagnosis, and is the basis of nearly all modern efforts to solve the problem. Hormones can and do pass the barrier of the placenta. Profound changes are produced in the pregnant woman's organ growth, circulation, skin, glands, etc.; she is often rejuvenated. Their origin must be in the fetus, a source of additional, possibly new and different, possibly even antagonistic hormones. If the fetus dies, these changes retrogress. There is no question but that a male hormone (using the singular for convenience) exists. There is some question when and in what quantity this hormone is first produced in the fetus. There is a still larger question if the male sex hormone, by circulating in the maternal blood stream, induces or can induce recognizable specific changes in the mother's body, by acting as an antigen with the production of "antibodies" or by some hormonal effect. Every cell of the male fetus must differ from the female cells of the mother. The mother has no organ homologous with the fetal testis or the fetal tissues that produce male sex hormone. There is probably no antagonism between sex hormones as such, i.e., they do not neutralize each other when mixed together. But there does appear to be some sort of antagonism, direct or indirect, between the specific hormone of one sex and the specific hormone producing organs or tissues of the opposite sex. Moore and Price reject Steinach's and other's ideas of sex hormone antagonism; they admit that certain facts do point to such action, but claim that the effect is indirect through the hypophysis. But compare the production of sterility by the parenteral injection of semen or even its vaginal absorption; the production of agglutinins against spermatozoa; and the occurrence of freemartins and other phenomena to be discussed in the immediately following paragraphs. Does the introduction of maleness, e.g., a male fetus, into the female body produce quantitative or qualitative changes that can, possibly one might add, some day in the future, be recognized by the clinician or the laboratory worker? Is there any evidence that a male pregnancy has an effect on the mother, different in degree or character from that of a female pregnancy? In the attempt to answer these questions, let us examine further evidence which is closely bound up with the inescapable idea of some sort of sex antagonism.

1. Ancient belief. This must be neither lightly regarded nor summarily ignored. The remarkable agreements of such beliefs among peoples widely separated in time, place and culture arrest attention. Somewhere in the welter, to be found some day by some seeing eye, may be a little, or *the* little, grain of golden truth. Not everything that we cannot prove scientifically is improbable.

2. The frequency of male abortions. The ratio of male to female abortions is at least 150 to 100. The cause must be in the "fruit." This may be the reason for nature's prodigality with male pregnancies, because so many are destroyed by some unfavorable reaction to their presence in the maternal organism. Some women seem to abort all male conceptions, carrying only female to term; the reverse, at least in my personal experience, is rare. Male stillbirths are also more common, even after discounting the usual causes for this condition and the hazards of male birth itself. Cases of unexplained and of "habitual" death of fetus near or over term are 80 per cent males. The excess of males among abortions and stillbirths is greatest during the first and last third of pregnancy; this may have something to do with the development of the interstitial cells in the fetal testis.³⁴ While it is true that there are more male than female twins (1043:1000; the ratio in single births, 1050-60:1000), due to the great preponderance of male pregnancies, the prenatal mortality of male twins is higher, and "as the number of individuals to a birth increases the relative proportion of males to females decreases." Nichols, who collected statistics of over 700,000 pairs of twins, has pointed out that the ratio of males to females decreases from 1059:1000 in single births to 548:1000 in quadruplets. The Dionnes are girls, and so are most quadruplets of press renown. In sheep there are over twice as many female as male triplets. For opposing view consult A. S. Parkes.

3. The occurrence of freemartins, in cattle and more rarely in other animals. A bovine freemartin, probably meaning "farrow heifer,"¹³ is the female co-twin of a normal bull calf; the female of two-sexed twins. Cattle breeders from Roman times have known that such females are usually sterile, 87 per cent or more (some observers claiming even 100 per cent) instead of the normal incidence of less than 10 per cent. Lillie has shown beyond all question that a freemartin is a "blighted" female calf fetus with undeveloped or deformed sexual organs (usually internal only), and often with more or less male characteristics due to saturation with antagonistic male sex hormone from its co-twin which interferes with the normal female development. This is possible, and occurs only when the chorionic or placental anastomosis between the binovular twins is early and extensive. Either the male shows an earlier sex differentiation and an earlier sex hormone production than the female, or the male sex hormone is more "powerful." The former of these ideas suggests that sex is not absolutely determined by the spermatozoon but is profoundly influenced by environment; the latter, again, the ancient thought of male superiority. Williams, in a personal communication, reports "Quintuplets with two males and three asexuals; triplets, one male and two asexuals, twins, one male and one asexual. Ten individuals with 4 males and six sexless. There were 8 abortions and two viable young (the twins)." Hartman believes that the process can be reversed in which a male co-twin is sterilized and made more or less asexual or intersexual (sexual intergrade) by the female. He calls these "reciprocal freemartins," and rather believes that both types do occur in man and may explain some cases of intersexuality (Novak). Contrary to a belief once held in rural England, no diminished fertility in the female of two-sexed human twins has been observed because a comparable placental

anastomosis does not occur in man. Sir J. Y. Simpson collected the married history of 123 women born co-twins with males and found that only 11 had no offspring.

4. Fetal malformations. As a whole, there are probably more male than female fetuses that are malformed. Dr. D. P. Murphy of Philadelphia, in a personal communication, says, "If you were able to secure figures on the sex ratio of 500 cases of any given type of defect you might well find . . . that the defects in most cases afflict the two sexes about equally." But the available figures show strange sex ratios of congenital deformities. Curiously enough, deformities of the brain and cord, and of congenital hip dislocation are much more common in the female. M. S. Michel of Minneapolis reported in 1928, 57 cases of *craniorachischisis*, of which 85 per cent were female; Malpas, 44 cases of *anencephaly* with 70 per cent females, and 80 of *hydrocephalus* and *spina bifida* with 57 per cent of that sex. Of 5,494 cases of congenital hip dislocation, 84 per cent were females. On the other hand of 3,309 club feet, 65 per cent were males. Of 507 cases of *harelip-cleft palate* gathered from various sources, 55 per cent were males. Ballantyne reports the sex ratio of his malformations as follows: *iniencephalus*, 1 male to 21 females (5 per cent males); *anencephalus*, 10 to 30; *genal fissure*, 41 to 26; *harelip*, 180 to 118; *diaphragmatic hernia*, 47 to 20; *preauricular appendages*, 21 to 12. These percentages are approximate. He states that there are more female *cyclopias* and united twins; but more male urinary umbilical fistulas and *polydactylism*; of *extroversion of the bladder*, male:female::"6 or 7:1"; of *transposition of viscera*, "2:1." I have not been able to secure much evidence for the suggestion that most *pseudohermaphrodites* are primarily males, the course of whose early sex differentiation has been altered by the antagonistic sex hormones of the mother. Such evidence would be very interesting. In 980 cases of *placenta previa* the male-female sex ratio was 124:100. While fetal malformations are not good witnesses to any distinctive effect of maleness on the maternal organism, still sex in some way would seem to play a part in their production.

5. Relation between male pregnancy and toxemia. An old belief, still alive, was that the pregnant woman vomits more if her baby is a boy. v. David suggests that the cause of the vomiting is something transmitted to the child from the father that is foreign to her blood; that the more the child resembles the father, the more the mother vomits; and that the pigmentation of the mother parallels that of the child. In all this, no direct mention of sex diagnosis. Herrmann reports in 1,442 cases of *eclampsia* a ratio of male to female children of 122:100 (normal ratio, 105:100); in the last four months of pregnancy, this ratio rose to 156:100; and in those *eclamptic* individuals with twins, to 173:100.

6. Serologic studies. These, while not conclusive, evidence a difference between male and female blood and serum greater than that afforded by chance.

The foregoing would seem to justify the conclusion that the introduction of the male element into the female body does produce effects. The mechanism by which the male fetus is protected against the antagonistic sex hormones of the mother is, at times, more or less broken down. Sufficient means and knowledge are not yet at hand to definitely recognize such effects and permit practical sex diagnosis.

The ancient ideas of the qualitative effects of a male pregnancy on the mother comprise a large number of "natural" means to diagnose fetal sex. Hippocrates said that "a woman with child, if it be a male, has a good color; if it be a female, she has a bad color." Ambrose Paré quoted this with approbation. It is remarkable that the agreement was so general that the appearance of the woman during a male pregnancy was good, with a sense of well-being. The face is brighter, the color better, the skin clearer; she is cheerful (Arabian), happy (Indian), and untroubled (Jewish). Many of these may be explained by the belief that the increased heat production, held to be associated with a male pregnancy, quickened the circulation and heightened metabolism; suggestion and wishful thinking may have played a rôle; finally, however, with these as with many other ancient ideas about fetal sex diagnosis, we may be standing on the edge of an unexplored field of endocrinology.

Freckles, pigmentation, and vomiting were sometimes stated to indicate a boy, though Hippocrates held that freckles meant a girl. While "liver spots," a blotchy skin and a bad or pallid color were usually interpreted to mean a girl, pigmentation in general pointed to a boy. There was widespread belief that *lack* of pigmentation of the linea alba below the navel meant a girl. The endocrinologists have here food for speculative thought. It was also an old idea that the desires of the pregnant woman are an expression of the desires or will of the fetus (and so helpful in fetal sex diagnosis), and that these fetal desires are often expressed in dreams. In India, if the pregnant woman dreamed of men's food, the baby would be a boy; in Russia, dreaming of a spring or well meant a girl; of a knife or club, a boy (Freud?). There was no agreement in the interpretation of changes in sexual desire during pregnancy. Incidentally, the subjective sensations of the pregnant woman have never been considered of great value as evidence in fetal sex diagnosis; but this may be another entirely unexplored clinical field.

The most interesting "natural" means in Group 3, anciently used to foretell sex, have been the supposed effects of the fetus on the pregnant woman's excretions: urine, milk, and sputum. A generation ago no one would have dreamed that the diagnosis of pregnancy was possible by an examination of the urine. But in ancient Egypt about 1350 B.C., according to the *Berlin Medical Papyrus*, both pregnancy and sex could be determined by this means. "To see if the woman is pregnant or not pregnant: barley and wheat are moistened daily with the woman's urine, like dates or pastry in two bags. If they either generate, so will she give birth; if the wheat germinates, so will it be a boy; if the barley germinates, so will it be a girl; if they do not generate, so is she not pregnant." The idea had found its way to Europe by the seventeenth century. "Make two holes in the ground, in one place some wheat, in the other barley, wet with the woman's urine and cover with earth. If the wheat sprouts first, the woman has a male fetus; if the barley first, a female." The test is mentioned in the old English book, *The Experienced Midwife*. Manger repeated the experiment in 1933 and reported 80 per cent correct prognostications, but his findings have not been corroborated. If any difference in the effect of male and female pregnant urine on the growth of these seeds *does* exist, it must depend on the presence of some substance produced, directly or indirectly, by the fetus.

There was a curiously widespread idea that the milk (sometimes specified as of the right breast) of a woman pregnant with a male was "tough" and thick. The test was to drop or squirt the milk onto a smooth surface, e.g. glass, a sword or a heated metal plate. If it remained conical or "stood like peas" or clotted, a male pregnancy was indicated; if it spread out or flowed off, a female. If some of the milk dropped into clear water or urine fell to the bottom, a boy was to be born; if it floated or dissolved, a girl. Another test was to knead the milk with meal into a small loaf to be baked over a slow fire; if it shriveled up or burned, a boy; if it "puffed up," a girl. It appears that these tests were occasionally, but much more rarely, applied to blood and urine. Much of the foregoing is not strange to primitive thought about sex.

With the two exceptions, marked vomiting which is still occasionally spoken of as a sign of a male pregnancy and sport with the pith ball, possibly the only other "natural" means to diagnose fetal sex, existing in popular thought today, are the changes that "old women" think they discern in the shape and appearance of the pregnant woman's abdomen and back. There is by no means complete agreement; but, in general, a hard, prominent, "high" and rounded abdomen and broad hips and back bespeak a male pregnancy. An abdomen sometimes described as "egg-shaped" is stated to indicate a female pregnancy. The origin and age of these ideas is not definitely known; some may have a phallic significance. While I have not been able to arrive at any definite conclusion from many wearied questionings and many observations, I am not willing to dismiss the matter as entirely without foundation. Possibly, an endocrine truth may be embodied in this popular persistent belief.

To digress a moment into veterinary medicine, cattle breeders have stated that the calf is more likely to be a male if the front quarters develop first in pregnancy and if the cow goes over term.

In modern times, excepting Frankenhaeuser's fetal heart study in 1859, there is no evidence that either science or scientific medicine concerned themselves seriously, if at all, with the diagnosis of fetal sex in utero, until toward the end of the first decade of this century. Since then the problem has been attacked from many angles. Those in Groups 1 and 2 have already been mentioned. In Group 3, serology and endocrinology have been the means employed; and the efforts, in the main, have followed the two ancient lines of thought about the effects of a male fetus on the maternal organism, the one, that they are quantitative; the other, that they are qualitative.

Excepting unsuccessful attempts to demonstrate a higher pH value in the blood of a woman pregnant with a male or a higher basal metabolic rate, the Manoilloff test is possibly the only modern example of the first idea, though not intentionally so in origin.

In ancient thought all things had sex, which the study of language amply illustrates. The alchemists held that the elements were male and female. E. O. Manoilloff, the Russian scientist, has revived that concept. He claims to be able to distinguish between male and female tissues and secretions (first in 1920), to determine the sex of the fetus by examination of the pregnant woman's blood, to diagnose the sex of plants, and to separate male from female minerals. He claims sex differentiation from stone to man. As a matter of fact, female sex hormone

has been recovered from minerals. Regarding fetal sex diagnosis, Manoilloff believes that a specific hormone from the fetal testis, or from the whole organism of the male fetus, passes into the maternal blood and changes its reaction. To the specially prepared blood is added an oxidizing agent, a reducing agent, an acid and an indicator. The result is determined by the absence or presence of a color reaction. The idea of many investigators is that this test represents an oxidation-reduction process, of which the former predominates in the male, the latter in the female; that the substances involved parallel the metabolic rate; and that the test is one of metabolic rate or level. It is quantitative, and not sex specific. We are back again at the beginnings; one mark of sex is a difference in metabolic rate. Many modifications of the test have been made and its chemistry is complex; the necessary technic is delicate and subject to much possible error. Manoilloff's claim of 80 per cent correct prognostications would seem overoptimistic.

A possible immunity reaction between the pregnant woman and her unborn male child has been the basis of most of the efforts of serology to solve the problem of fetal sex diagnosis during the past twenty-five years. It follows the second ancient idea that one of the effects of a male fetus on the maternal organism is a qualitative change, caused by the elaboration of specific substances, and is predicated on the four following assumptions: (1) Even early in pregnancy there is sex differentiation in the fetus (morphologically, sex can be distinguished in a fetus 20 mm. long and six weeks old), which becomes more marked as pregnancy advances. (2) The male secretions, i.e. the "maleness," of the fetus passes into the mother's blood. (3) These secretions, being "foreign" to her body cells and their products, act as antigens. (4) As a result the mother produces "antibodies" against the invading "foreign" substances. The demonstration of these hypothetical "antibodies" has been attempted by precipitin reactions, agglutinations, complement fixation tests, activity of ferments and allergic phenomena. The possibility must be constantly borne in mind that all such serologic tests may be invalidated by previous sensitization.

Petri experimented with precipitin reactions between cow and steer serums and steer testis extract. Both serums gave precipitations when overlaid with the steer testis preparation, though stronger with the steer serum. The same results were obtained when antitesticular serum (from rabbits injected with this testis preparation) was tested against cow and steer serums. Even after fractional precipitation of this antitesticular serum by cow serum until precipitation ceased, the addition of steer serum still gave a reaction. By these and other reactions he was able to determine the sex of serums in many cases, but the test was not dependable. Abraham in 1912 to 1914 conducted an extensive series of precipitin experiments. He injected rabbits with male and female pregnant serums and with male and female nonpregnant serums. Combinations and dilutions of serum from these sensitized rabbits were tested for precipitation against serums similar to those injected. His results were also not conclusive. His work stimulated investigation and his article contains an extensive bibliography.

The agglutination or immobilization of animal and human spermatozoa by the serums of pregnant women has been briefly investigated by me. While the degree of the reactions varied from what might be called complete to none whatsoever, even the markedly positive cases did not seem

to be of value in fetal sex diagnosis. Of course, it can be argued that spermatogenesis is not a function of fetal life; that it is not known to what degree "maleness" is dependent on the external secretion of the testis; and that the serums might have been from patients already sensitized. References to other work of this character have not been found.

Complement fixation tests for diagnosing fetal sex were employed by Petri, using extract of fetal testis, inactivated navel blood, and fresh guinea pig complement. All gave hemolysis. Others have tried to solve the problem by this method which would seem to merit further investigation. I had a personal interview with an individual who believed that he had succeeded by this method. The New York Academy of Medicine scheduled for the Section of Obstetrics and Gynecology on April 28, 1925, a paper by Isaac Fried, M.D., entitled "The Serodiagnosis of the Sex of the Fetus During Pregnancy," "by invitation." The paper was withdrawn before the day of the meeting arrived. The author's interesting, but not at all convincing, complement fixation test, featuring a very complicated, possibly even fantastic, antigen, was published in the *Medical Review of Reviews*, August, 1924. He claimed 100 per cent correct prognostications.

The principle of the Abderhalden test [the formation of protective (?) ferments against living foreign proteid] has been extensively used in trying to foretell fetal sex, using testis instead of placenta. Waldstein and Erkler in 1913 reported positive results from the action of pregnant serum on testis, but they considered it due to previous semen absorption and made no mention of its possible use in fetal sex diagnosis. In 1914 Franz Lehman first suggested that fetal sex might be determined by a modification of the Abderhalden test. Later, he attacked the problem himself. Koenigstein of Schauta's clinic in Vienna in 1913 found that there was more destruction of fetal, infant, and steer testis by male than female pregnant serum. In 1917 Kraus and Saudek of Bruenn published their stimulating work done in 1913 and 1914. They employed carefully prepared (kosher) steer testis and pregnant serum, claiming nearly 80 per cent correct prognostications. Schaefer of Bumm's clinic tested fetal and adult human testis and calf testis with pregnant serums; the best results were obtained with fetal testis, but the conclusion reached was that the test was not reliable. The most determined effort to use a modified Abderhalden test in fetal sex diagnosis was made in 1924 by Luetge and v. Mertz at Sellheim's clinic, the scene of Abderhalden's original work. For a "substrat" they used carefully prepared bull testis (later, a commercial product free from aminoacids), which was incubated with the serum to be tested. The high molecular proteids were precipitated from the filtrate by alcohol, using this instead of dialysis. After further filtration, the final fluid was tested for split proteids, presumably produced by the antitesticular ferments in the male pregnant serum, by a ninhydrin color reaction. In 1925 I spent a day in their laboratory, and, later in the same year, tried to duplicate their results at the Kilmer Pathological Laboratory. Our first seventeen serums were diagnosed (?) correctly; the next eight were wrong. A large literature for and against the method and its accuracy exists. The originators claimed over 78 per cent, even up to 98 per cent, correct prognostications. Those interested may consult their book. The optical interferometric method of Loewe-Zeiss has been used by many investigators, especially P. Hirsch, to test the serum after incubation, quantitatively.

Allergic skin reactions have been the basis of a number of attacks on the problem of fetal sex diagnosis. Lehman tried skin inoculations with extract of animal testis; Koenigstein cutaneous injection of testicular extract in pregnant animals and pregnant women. Their results were not definite. Human semen and extracts thereof, preparations of testis (both animal and human) and male fetal blood serum have been employed in skin tests on pregnant women by scarification and intradermal injection. The reactions have been sometimes negative, sometimes slightly to markedly positive, frequently bizarre. While the results have been too conflicting to permit definite conclusions as to their ultimate value in prognosticating fetal sex, they have been without question better than those afforded by chance. The most recent report is by Davis who injects intradermally a stock testicular extract, grades the test by the resulting wheal and reports between 80 and 90 per cent correct findings. It is a hope that all these puzzling skin reactions may be better understood when the workers in allergy shall have been able to put their house in order.

Although fetal sex hormones must be the primary cause of any differences that may exist in the effect of fetal sex on the pregnant woman, endocrinology to date has disappointed high hopes of solving the problem of fetal sex diagnosis. The male and female sex hormones are closely related chemically, their differentiation in the blood is difficult, and "both male and female stimulating substances can be extracted from both male and female urines" (personal communication from Dr. Carl R. Moore). With the cooperation of Mr. Jesse Briggs of the Kilmer Pathological Laboratory, I have carried on some observations of the number and prominence of the developed follicles in the Friedmann test, to determine any relationship to the sex of the child. The number of observations has been too small to warrant any conclusion. Dorn and Sugarman injected intravenously into immature male rabbits, whose testes must be in the inguinal canals and not in the scrotum, the urine of woman pregnant in the last trimester of pregnancy. If later examination of the testes of the animal showed increased vascularity and cellularity and beginning spermatogenesis, they believed that they could conclude from their series of cases that the woman was pregnant with a female fetus. They thought that they had discovered, in the urine of women carrying a female child, a true and hitherto undiscovered sex "hormone which can stimulate the cells in the testicular tubules of the pubescent male rabbit and cause a precocious development." They claimed 94 per cent, 80 out of 85 cases, correct prognostications. Other workers have not been able to duplicate their results. Mathieu and Palmar cite numerous references, record the results of their own investigations which did not succeed in accurately diagnosing fetal sex, and indulge in some interesting speculations. It was inevitable that the hormone test for pregnancy would be employed in the attempt to solve the problem. It is encouraging to remember that endocrinology is the merest infant in the world of medicine.

SUMMARY

All efforts ever made to diagnose the sex of the human fetus in utero may be placed in three groups.

In the first group are the beliefs that the male comes from the right side of the uterus or the right ovary, and that male pregnancies cause right-sided symptoms in the mother.

In the second group are the beliefs that the physical attributes of the fetus during pregnancy and labor differ in the sexes.

In the third group are the beliefs that the male fetus, through its secretions, affects the mother differently than does a female fetus. These differences in effect may be of degree or kind, and there is some evidence that they do exist. Sufficient knowledge and means are not now at hand to recognize these differences for practical use. This group is the largest.

The ancient beliefs about the diagnosis of fetal sex have almost entirely disappeared, but are of interest, for ancient thought is the basis of nearly all modern attacks upon the problem.

Modern investigations of the problem have one or more representatives in each group. In the third group serology and endocrinology have been the means employed, with encouraging results.

That much thought has been expended and much work done in this broad field, with its many converging paths of research, is evidenced by the appended bibliography, which is by no means complete.

Neither clinical observation, nor serology, nor endocrinology has solved the problem of fetal sex diagnosis.

CONCLUSION

The correct prognostication of fetal sex would satisfy a great curiosity and answer the pregnant woman's age-old question. It is true that it would not have great practical value. Research along other lines might well produce more solidly beneficent results. It may be true that such diagnosis, if possible early in pregnancy, might increase the incidence of induced abortions, though this does sound a bit timorous and far-fetched. The parents made unhappy by knowing beforehand what they were going to have might easily be outweighed by those rejoicing in the knowledge that they would have a child of the sex they most desired. Its discovery might be exploited by the unscrupulous, as was salvarsan in its early history. All these and other objections have been raised. But the fact remains that no permanent harm has ever come by making the way of truth wider or smoother or straighter, or by pushing it a little farther. The diagnosis of fetal sex in utero is one of the unsolved problems of obstetrics. As such, it will remain a challenge. Some day, some eye will see clearly what men have, as yet, seen only through a glass darkly; or some laboratory worker will present the answer to us face to face. Clinical observation may come into its own some day, and what lies ahead in hormone study is not even dreamed of. The problem may still be solved.

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Department of Book Reviews

CONDUCTED BY ROBERT T. FRANK, M.D., NEW YORK

Review of New Books

Gynecology

Dr. Jameson has given us a delightfully written account of the early customs and manners in obstetric practice and teaching, as well as depicting the rise of the recent specialty of gynecology, in this newest example *Gynecology and Obstetrics*¹³ of the series of histories which have been appearing under the title of "Clio Medica."

Evidently in obstetrics as in other branches of science little that we think is new is really new, for as the author carries us through the traditions and customs of the early period and those of Greek and Roman times we find many suggestive allusions to methods which are not far different than those of the present day. What a commentary it is on the profuse output of the obstetric and gynecologic texts of this era to read that the famous "Rosengarten" of Eucharius Roslin was the first obstetric textbook to be issued in fourteen centuries.

The modern period of obstetrics begins with the work of Mauriceau, van Deventer, and Portal, and from this we are gradually carried to the development of the modern maternity hospital. One of the most interesting chapters in the book is the account of the Chamberlain family, and the development of the obstetric forceps. The story of puerperal fever is no less interesting, especially in view of the fact that sepsis still remains the scourge of modern maternity. It is especially pleasing to note the large part which American surgeons took in the development of gynecologic technique. The obstetric classics, in many instances consisting of records of the original procedures and discoveries, are reviewed. This most interesting contribution to the history of obstetrics and gynecology deserves to be widely read.

—Philip F. Williams

Gynecological Operations,¹⁴ and their topographic anatomic basis, by Martius, gives a survey of the gynecologic technique as practiced at the Goettingen Gynecological Clinic. In his foreword the author promises to give a short operative gynecology, mainly based on topographic anatomy, designed for both students and physicians, together with a brief text giving the pathologic background. It may be said that he has succeeded in performing this difficult task in an almost faultless fashion.

The text is illuminated by 404, chiefly colored, halftones, clearly drawn and well executed. I know of no other operative gynecology which is more clearly designed or better illustrated. Throughout, the author uses conservativeness and good judgment for indications of the operation. The topographic anatomy is not concentrated in one portion of the book, but distributed with each operation so that it is immediately available during the reading of the text. The schematic drawings are of utmost value.

¹³*Gynecology and Obstetrics*. By Edwin M. Jameson, M.D., Surgeon, General Hospital, etc., Saranac Lake, N. Y. 170 pages with 5 illustrations. Paul B. Hoeber, Inc., New York, 1936.

¹⁴*Die Gynaekologischen Operationen*. Von Professor Dr. Heinrich Martius, Direktor der Universitaets-Frauenklinik in Goettingen. 396 Seiten, mit 404, zum groessten Teil farbigen Abbildungen und Bilderreien. Verlag von Georg Thieme, Leipzig, 1937.

In the operation for fibroids he counsels the retention of the cervix unless special indications for complete hysterectomy are found. Unlike so many German authors, he does not approve of re-infusion of the blood shed into the peritoneal cavity in ectopic gestation but prefers a donor for the transfusion.

In the treatment of tuberculosis of the adnexa he favors small, frequently repeated dosage of x-ray. In unilateral ovarian malignancy, he advises bilateral oophorectomy and hysterectomy unless the indications for limiting the procedure are very strong.

In the operation for tubal ligation, he describes the inguinal canal route in utmost detail with 19 illustrations. There are also numerous operations described for the treatment of malpositions of the uterus. In the treatment of cystocele, although the technique includes careful separation and elevation of the bladder, a modified Stoltz circular suture is still employed. He likewise exposes the levators and sutures them together in perineorrhaphy.

Although one may differ in minor details and have preferences for modification of technique, it is a pleasure to read this book and to study its excellent illustrations.

—R. T. Frank

The purpose of this small work, *Urology in Women*,¹⁵ is to present only the urologic lesions peculiar to women. The incompleteness necessitated by such an intention rather limits the usefulness of the book by making it an adjunct to larger works on surgery or urology.

In revising the text an interesting discussion of the rather rare lesion of endometriosis of the bladder has been included, as well as a section on vesical neck obstruction. Among the notable revisions are the discussion of changes in the ureters during pregnancy and menstruation, the dietary treatment of pyelitis and on nephroptosis. There is a marked tendency to recommend proprietary therapeutic agents by their trade names.

The subject matter is well handled and the book should be useful, though in no sense a work of reference.

—Philip F. Williams

*The Results of Ovarian Grafting*¹⁶ is a report presented by Mocquet and Cotte before the Forty-fifth Congress of the French Surgical Association. The subject of this monograph is divided into 2 main parts, the first dealing with experimental grafts by Mocquet, the second and larger portion with surgical grafts in the human being by Cotte.

This short monograph will be found of great use for anyone interested in finding the literature and the results obtained in ovarian grafting. The conclusion that homographs and heterographs are rarely of value is in keeping with the general experience of the profession.

—R. T. Frank

Schubert in a small monograph¹⁷ describes the technic of his operation for the establishment of an artificial vagina. His material comprises 32 patients operated upon, with one death. The operation, beautifully illustrated, utilizes the lower portion of the rectum for the artificial vagina. Then, through the sacral route, the upper portion of the rectum and sigmoid are drawn down and sutured, within the anal sphincter, to the skin.

¹⁵*Urology in Women*. By E. Catherine Lewis, M.S. (Lond.), F. R. C. S. (Engl.), Surgeon to Royal Free Hospital, etc. Second edition. Illustrated, 100 pages. William Wood & Company, Baltimore, 1936.

¹⁶*Résultats des Greffes Ovariennes*. Pierre Mocquet de Paris et Gaston Cotte de Lyon. 126 pages. Association française de Chirurgie, XLV Congrès française de Chirurgie, Paris, 1936.

¹⁷*Die Kuenstliche Scheidenbildung aus dem Mastdarm*. Von Dr. Gotthard Schubert. 69 Seiten mit 35, teils farbigen Abbildungen. Ferdinand Enke Verlag, Stuttgart, 1936.

The case which speaks most highly in favor of this method is that well-known one of Wagner who performed the operation of Schubert in a patient in whom the vagina had been entirely destroyed by postpartum sepsis. Later this patient delivered 3 children through the newly made canal.

The author has made no attempt to gather the literature in order to determine the actual mortality following his type of operation.

—R. T. Frank

Mathey-Cornat has covered *Gynecological Radiotherapy*¹⁸ in a well-written monograph. There is a short introduction on technic and dosage, cautions to be employed, the dangers and bi-effects which may be encountered.

Radiotherapy is recommended for endometriosis, both pre- and postoperatively in the treatment of fibroids. He prefers daily fractional dosage extending over twenty to twenty-five days. He wisely excludes any doubtful cases and also young patients in whom myomectomy could be performed. He concludes that failures are rare unless based on the wrong diagnosis.

For uterine bleedings in the young as well as for permanent sterilization, his choice is radium in preference to x-ray. In tuberculosis of the genitals his results have been good. As most other men in this field, he believes that operable corpus carcinoma should be treated by surgery.

Both for sarcoma of the uterus and for chorionepithelioma as well as for ovarian malignancies, he advises only postoperative radiations. For carcinoma of the breasts, pre- and postoperative radiation is used.

The monograph is well illustrated. It incorporates in its pages much of the world's literature referring to the subject.

—R. T. Frank

The seventh volume of *Ergebnisse der medizinischen Strahlenforschung*¹⁹ is the first one to appear since 1933. It contains a fund of interesting material. The 12 articles with the exception of 2 from Zürich and 1 from Czechoslovakia, are all from Germany. The first one deals with dextroversion of the aorta, a condition rarely giving symptoms, usually an accidental x-ray find but sometimes causing esophageal or tracheobronchial disturbances. The next takes up Hand-Christian-Schüller disease. One hundred and forty cases have been reported in the literature. The defects in the membranous bones, diabetes insipidus, and exophthalmos, as well as xanthematosis, give a clear-cut clinical picture. Good effects are reported from x-ray therapy.

Osteosclerosis fragilis generalisata, the so-called Albers-Schoenberg "marble bones," is a disease existing from earliest infancy, showing diffuse osteosclerosis, fractures due to fragility, and change in the blood morphology—anemia, hemoglobin even down to 20 per cent, micro- and macro-erythrocytes, poikilocytosis, etc. Enlarged posterior clinoids, optic atrophy, and sequestration of the lower mandible may be noted. The blood calcium is usually doubled. No evidence that the parathyroids are involved has ever been offered.

Osteopoikilie—"osteopathia condensans disseminata"—of which 72 cases are on record, recognized by the punctate or linear striation of the bone, often accompanied by scleroderma and dwarfism, is described. Another interesting condition is myositis ossificans progressiva which in 62 to 70 per cent is accompanied by microdactyly.

Of various other conditions described may be mentioned lung atelectasis, perforation of the kidney pelvis and ureter during pyelography without severe clinical symp-

¹⁸*Radiothérapie Gynécologique*. Par R. Mathey-Cornat, radiologiste des hôpitaux, etc. 369 pages. Masson et Cie, Paris, 1936.

¹⁹*Ergebnisse der Medizinischen Strahlenforschung*. Herausgegeben von Holfelder, Holthusen, Juengling, Martius und Schinz. Band VII. 622 Seiten mit 294 Abbildungen im Text. Verlag von Georg Thieme, Leipzig, 1936.

toms, and tuberculous adnexitis in which 80 per cent are cured by x-ray therapy. On the other hand, in nonmalignant uterine bleeding radium is preferred to roentgen rays.

The last 3 papers deal respectively with the treatment of esophageal carcinoma, lymphogranulomatosis, and radiotherapy in the treatment of mammary carcinoma. The reproductions of the x-ray photographs which play a large rôle in the description are extremely good.

—R. T. Frank

The second edition of *Gynecology for Nurses*²⁰ by the Drs. Crossen is a well-planned, attractively prepared book. It is well designed for study and teaching, profusely illustrated, and covers the subject in a very readable fashion because of its precision and directness.

Particular attention has been paid in this new edition to our most recently acquired knowledge of physiology, especially to that of the ovary and the pituitary. There is a very clear chapter on endocrine disorders.

—R. T. Frank

*Prostitution*²¹ by Tage Kemp is based on investigations made in Copenhagen, partly financed by the corporation of the city and partly by the Rockefeller Foundation. The text deals with the abolition of the regulations of prostitution in Denmark, as well as with the laws now in effect. The very evident fact that only 29.4 per cent of those examined were mentally normal and without defective intelligence is emphasized. This is a serious contribution to the subject.

—R. T. Frank

The second edition of Kahr's *Conservative Therapy of Women's Diseases*²² follows the first after an interval of only two years. The author has covered the field very fully in such a fashion that either the general practitioner or the specialist can readily find all the current methods applicable to a given condition. In this new edition such advances in hormonal therapy as have been developed in the last few years have been incorporated. In the treatment of infantile gonorrhea, just as in this country, exhibition of large doses of estrogenic substance is advocated. For the cure of gonorrhea, however, I see no mention of hyperthermia, a new method which is being used in this country with increasing frequency and good results. As so often is the case in books of this type, a huge number of prescriptions are incorporated in the text.

—R. T. Frank

The second enlarged edition of Hans Runge's monograph on *Bleeding and Leucorrhea*²³ appears as Volume IX of *Medizinische Praxis*, a series for post-graduate education of physicians.

The second edition takes full cognizance of the changes in our knowledge of functional bleeding based on hormonal investigations.

²⁰*Gynecology for Nurses*. By Harry Sturgeon Crossen, Professor Emeritus of Clinical Gynecology, Washington University School of Medicine, etc., and Robert James Crossen, Instructor in Clinical Gynecology and Obstetrics, Washington University School of Medicine, etc. Second edition, with 357 engravings including one color plate, and 316 pages. The C. V. Mosby Co., St. Louis, 1936.

²¹*Prostitution*. By Tage Kemp, M.D., Copenhagen. Translated from the Danish by Elsie Marie Werner Kornerup. 253 pages. Levin & Munksgaard, Copenhagen, 1936.

²²*Konservative Therapie der Frauenkrankheiten*. Von Professor Dr. Heinrich Kahr, Vorstand der I. Universitäts-Frauenklinik in Wien, etc. Zweite, neubearbeitete und vermehrte Auflage. 327 Seiten. Verlag von Julius Springer, Wien, 1937.

²³*Blutung und Fluor*. Von Professor Dr. Hans Runge, Direktor der Universitäts-frauenklinik, Heidelberg. Zweite, erweiterte Auflage, mit 18 Abbildungen auf 117 Seiten. Verlag von Theodor Steinkopf, Dresden, 1936.

The second portion of this short monograph is a description of causes of leucorrhea and its treatment. Little new has been added to our knowledge for the relief of this unpleasant symptom.

—R. T. Frank

*Facts and Frauds in Woman's Hygiene*²⁴ by Rachel Palmer and Sarah K. Greenberg is a medical guide for the laity against misleading claims and dangerous products. It is well written, terse, and hits straight from the shoulder. There is no hesitation in mentioning innumerable products which have gained a large number of users simply through misleading advertising. In addition, the various subjects discussed should give the reader additional insight. The entire realm of "feminine hygiene" including menstruation, dysmenorrhea, irregularities, leucorrhea, sterility, and contraceptives is taken up. Certain particularly dangerous drugs such as those containing amidopyrine are singled out. The book should fulfill a want for those who are in doubt about many of these subjects, among whom I am loath to confess many physicians must be included.

—R. T. Frank

Sex Problems

Havelock Ellis has written a *Psychology of Sex*²⁵ as a manual for students. In this comparatively short volume of 377 pages, he has compressed the contents of his seven preceding treatises. As heretofore he emphasizes the normal phenomena of sex and shows how wide a frontier exists between the normal and the abnormal.

The statement that in scientific knowledge of sex, physicians are often less informed than their patients, must be conceded as true. He describes the biology of sex, including its determination by the chromosome, the intersexual form, hormonal deviations in later life, the sex impulse itself, the erogenous zones, and the periodicity of sex impulse, furthermore, the relation of the 5 senses to sexual impulses.

He next takes up children, particularly libido as a general manifestation. In children there can be no homosexuality where there is not as yet a conception of sexuality. The discussion includes such well-known matters as the Oedipus complex, masturbation, narcissism, etc., in detail. The sexual impulse in youth and sexual deviations in the adult are described and analyzed. Among the main contents of the book are chapters on marriage and the art of love.

This very sane treatise which does not attempt to enter into the subject of psychoanalysis, although it does not deny its applicability in appropriate cases, is not only of extreme value to the student, but should be in the library of physicians as well.

—R. T. Frank

*The Single Woman and Her Emotional Problems*²⁶ is a sympathetic study of the psychologic difficulties of the large group of more or less independent single women who are forced to live out their lives as best they can without the natural fulfillment of their normal physiologic functions. To this group of women with sympathy and an evident understanding the book is offered.

The author discusses the origin of this group of women which she feels results from the further education of women, their professional training and in part the aftermath of the dislocation of society following the World War. She discusses the

²⁴*Facts and Frauds in Woman's Hygiene.* By Rachel Lynn Palmer and Sarah K. Greenberg, M.D. 311 pages. The Vanguard Press, New York, 1936.

²⁵*Psychology of Sex. A Manual for Students.* By Havelock Ellis. 377 pages. Emerson Books, Inc., New York, 1935.

²⁶*The Single Woman and Her Emotional Problems.* By Laura Hutton, Physician. Institute of Medical Psychology, London. William Wood & Co., Baltimore, 1935.

friendships which arise between members of these groups, often sad substitutes for the companionship of marriage, remedies for loneliness, attempts to satisfy maternal instincts and other emotional states. Her handling of the psychologic problems involved gives excellent advice to women who have joined in a friendship unequal in one respect or another.

The author very sanely discusses the sexual problems of the single woman and their relationship to her unfulfilled wifehood and maternity. Her discussion of masturbation and homosexuality is clear and easily understandable by the lay person and should be of great help in the instances where such problems are presented for solution. Sexual inversion and other perversions and neuroses of a similar type, as well as alcoholism and drug addiction are analyzed, not only from the point of origin but as well of treatment.

In concluding the book, the author recapitulates the adjustments which may have to be made by many single women in their relationships to other women. She very wisely denies that the adoption of a child could be considered a suitable remedy for many of the problems of the single woman. She suggests many ways in which sexually unexpended emotional energy may be distributed in numerous and varied interests. This is an excellent book to be read by the single woman herself, by her medical advisor, and by her religious advisor.

—Philip F. Williams

The Married Woman,²⁷ written in collaboration by a well-informed sociologist and a physician, who is also a gynecologist and teacher, comprises a very practical volume for married women, with a clear and sane discussion of the various problems and situations which frequently confront her. The book begins with the physiologic and psychologic attitudes and inhibitions of postpuberty and early maturity period which influence the woman in marrying or not marrying. There follows a consideration of the right attitudes for the woman who is to be married, bringing out an especially important point, namely, the health of the two parties to the marriage and the significance of various diseases in their future intimate union. This chapter forms an excellent basis for the education of the physician who may be consulted for premarital advice. The physical relationship of marriage is described in a succeeding chapter with particular reference to mental as well as physical adjustments in the marriage act. As the book proceeds the problems of the "seasoned wife" and the common problems of marriage such as family relationship, her husband's business interests, her own gainful employment, as well as the marital relationship, are taken up. The advice is practical in every respect.

The subject of motherhood and woman's fitness for motherhood particularly, with regard to the state of her health as well as that of her husband, with a pointed passing reference to induced abortion, makes the subject matter of an excellent chapter. The hygiene and physical changes of pregnancy, the subject of prenatal care and delivery are simply described but with emphasis on necessary points of value. The re-adjustments when the wife becomes a mother is plain common sense. For the married woman who remains sterile, the chapter on the childless wife with its excellent advice as to overcoming the mental frustrations in the completely sterile woman will be of help. The book proceeds with a discussion of the period of age fixation and the time of the menopause and describes the mental and sexual maladjustments and changes which are often present at such times.

This book may be heartily recommended to all women and the reading of it will tend to a more sympathetic understanding by the physician of both the mental and sexual problems which his married patients may bring to him for solution.

—Philip F. Williams

²⁷*The Married Woman*. By Gladys H. Groves and Robert A. Ross, M.D. 278 pages. Publishers: Greenberg, Inc., New York, 1936.

This discussion of *Contraception as a Therapeutic Measure*²⁸ concerns the 1,152 dispensary patients referred to the Bureau for contraceptive advice in Baltimore by physicians. Since this survey was conducted in a southern city it is somewhat surprising that only one out of five patients was colored. In any study of the use of contraceptives it is generally believed that the patient must be intelligent enough to understand a rather exact technic, and it is interesting to note that Dr. Moses considers that 60 per cent of her patients had a low degree of intelligence and only 4 per cent had a high degree of intelligence. She states that contraceptives had been used previously by many of her patients before they had been referred to the Bureau and only 15 per cent had any success in their attempts to limit their families.

A noteworthy fact brought out by the study of this group of women shows that there has been a very high abortion rate; approximately 37 per cent of the 981 nontherapeutic abortions were admitted to be either criminally or self-induced, and the average number of abortions per patients had been 2.1 per cent.

In a group of women advised as to methods recommended, namely, the vaginal diaphragm, vaginal jelly, and douche, only 2.1 per cent of the total treated patients were actual failures, and in a group who became pregnant, a gross number of 234, roughly 71 per cent, were women of low intelligence. In the women who became pregnant, either the method advised had not been used or ineffective material or faulty technic seemed to be responsible factors. Over 22 per cent of the patients treated could not be located for follow-up work. A noteworthy finding was the physical and mental improvement observed in many women due to the respite from childbearing and relief from fear of pregnancy. No definite injury or sterility was noted following the use of the method.

This Bureau began with a very definite purpose of studying women in whom physicians felt contraception was advisable and this small book represents the worth while factual presentations of the work done. To those who are interested in the statistical aspect of birth control this book will be of value.

—Philip F. Williams

This *Medical History of the Control of Conception*²⁹ gives a comprehensive review of the age-long and world-wide attempt, for one reason or another, of all peoples to limit reproduction. In such a widely collective study, the social and economic imputations are of almost equal interest with the medical and historical items presented. The book appears under the aegis of the National Committee of Maternal Health, one of whose members, Dr. Dickinson, has written a friendly foreword in which he implies that organized medicine has sidestepped its responsibilities in not taking an active part in the discussion of this vital problem of control of conception.

The material is divided in six parts. Contraceptive technique before the dawn of written history discusses the known or traditional practices of preliterate societies. It is evident that while the desire was wide the practice of contraception was narrow, and the population was limited, if not by disease then by abortion, infanticide, or sexual taboos. Through antiquity, Egyptian papyri, the ancient Jewish books, and the writings of the early Greeks and Romans the discussion of the problem in its various aspects is traced. Among the available sources of early eastern cultures the tenuous thread is followed in China, Japan, and India, and pursued through the manuscripts of the Islamic period of medicine and the folk beliefs and lay literature of the middle ages. It is of passing interest to note that the etymology of the word "condom" has not been solved.

²⁸*Contraception as a Therapeutic Measure.* By Bessie L. Moses, M.D. 90 pages. The Williams & Wilkins Company, Baltimore, 1936.

²⁹*Medical History of Contraception.* By Norman E. Hines, Ph.D. Illustrated, 521 pages. The Williams & Wilkins Company, Baltimore, 1936.

After a review of the recent past, the trials, the handbills, and the notoriety period, ending in the story of the career of Margaret Sanger, the author brings one to the best of the book, a philosophical sociological analysis of the present status and technic of birth control with reflections upon the ethnic and political angles and possibilities of this world-wide movement. The documentation of the book is sweeping in its inclusiveness; there are over seventy pages of author and source references.

This book will rank high for years as a reference work in this particular field of medicine and sociology.

—Philip F. Williams

The Single, the Engaged and the Married,³⁰ by Maurice Chideckel, does not strike the right note. It appears to overemphasize sexuality, even for a book of its kind. The physician reader will find it replete with errors. Such a statement as appears on page 37, "fourteen women past thirty-five had each a fibroma, or benign tumor, of the uterus. They had the tumor because they were not married, a high price for not obeying the laws of Nature," is a fair example. The book is unsuited to the lay reader because of the accentuation of sex abnormalities which would prove misleading.

—R. T. Frank

The Physician

No more delightful book³⁵ can be put in the hands of a last year medical student or a young doctor waiting for patients soon after he has started in practice, than this mellow, understanding book written by Wingate M. Johnson. It is entitled *The True Physician* with the subtitle *The Modern "Doctor of the Old School."* It lives fully up to its title. This book is based on lectures to the graduating class of Duke University. Among other things, it contains the principles of ethics of the American Medical Association.

Included in the topics discussed are the interne locating for practice, the modern family doctor, the choice of general practice, specialization, group practice, or public health work.

Most understandingly the author discusses the early days of practice. It is replete with valuable advice. Among other things, he warns against the drug addict and the woman seeking abortion who drift into the doctor's office. The doctor as a citizen, the business side of practice, contacts with law and courts, and even the personal side of his life, contemplated marriage, social relations are taken up. The final chapter discusses what reading young medical men can do, not only medical but cultural. Altogether delightful reading.

—R. T. Frank

Volume I, No. 1 of *Medical Classics*,³⁶ compiled by Emerson Crosby Kelly, contains a short biography and a full bibliography of Sir James Paget. In addition the full text of the three best-known contributions of this famous physician and scientist is given in full with reproduction of the original illustrations. This includes "On a Form of Chronic Inflammation of Bones (Osteitis Deformans)," "Additional Cases of Osteitis Deformans," and "On Disease of the Mammary Areola Preceding Cancer of the Mammary Gland."

This makes accessible in very attractive form these contributions which are now difficult to refer to and which today are as important as when they were published.

³⁰*The Single, the Engaged and the Married*. A treatise on the mutual adjustment for the attainment of happiness in marriage. By Maurice Chideckel, M.D., 268 pages. Eugenic Publishing Co., Inc., 1936.

³⁵*The True Physician*. The Modern Doctor of the Old School. By Wingate M. Johnson, M.D. 157 pages. The MacMillan Co., New York, 1936.

³⁶*Medical Classics*. Compiled by Emerson Crosby Kelly, M.D. Department of Surgery, Albany Medical College. The Williams & Wilkins Co., Baltimore, 1936.

The subjects which will appear in successive issues are of equal historical and immediate interest. I mention only a few: Addison's disease, Banti's disease, Dercum's disease, and Mikulicz's disease.

—R. T. Frank

Dr. Jacoby, who has previously discussed the interrelation of law and medicine, and education and medicine, considers in *Physician, Pastor, and Patient*³⁷ topics of mutual concern to medicine and religion. The openminded presentation of the many subjects should promote a better understanding and cooperation of the two great forces aiming at human betterment.

The first part of the book is devoted to an historic and philosophic reflection upon the development and practice of modern medicine. In the second part of the book, the effect of superstition upon medicine, the relation of various forms of religion to the general problems of hygiene and health are discussed, and chapters on the patient's faith and the inexplicables in medical practice are introduced. The third part of the book deals directly with such vital problems as may be presented to the physician and clergyman simultaneously. As Dr. Jacoby says the relationship is connoted by the cry of the tragedy-stricken home "telephone for the doctor and send for the priest." Here he takes up contraception and artificial abortion, the divorce problem, sterilization, sex education, euthanasia, vivisection and the problem of privileged communications. These sections present a well-thought-out argument, pro and con, to help the medical and religious adviser where such problems arise and their counsel is sought.

This stimulating presentation may be profitably read by both physicians and ministers in order that they may develop a rational meeting ground in their mutual problems.

—Philip F. Williams

*Medicine and Mankind*³⁸ is a series of seven lectures given at the New York Academy of Medicine by prominent physicians for the instruction of the lay public. A wide field is covered. The subjects are such diverse topics as: How We Learned About the Human Body, Medicine in the Days of Louis XIV, Contributions to Medicine of the American Aborigines of Both Continents, Constitutional Factors in Disease, Organic Background of the Mind, Vitamins, and the Mystery of Death. Both the lay public and physicians will find this interesting and instructive reading.

—R. T. Frank

Miscellaneous

*Syphilis and Its Treatment*³⁹ is a timely book. There are many treatises on syphilis but with the present program of the Public Health Services and associated institutions to make a concerted drive to eradicate this needlessly common disease, there is, as the author states in his preface, a need for a clear, simple and relatively complete account of the disease and its treatment. The author has admirably succeeded in this aim.

In reviewing the book for this special journal one may omit the generalities of the topic and examine the portions of the book relating to obstetrics. It is noteworthy that aside from a discussion of the site of the initial lesion in the female,

³⁷*Physician, Pastor, and Patient*. Problems in Pastoral Medicine. By George W. Jacoby, M.D. 390 pages, illustrated. Paul B. Hoeber, Inc., New York, 1936.

³⁸*Medicine and Mankind*. Lectures to the Laity delivered at the Academy of Medicine in New York. Edited by Jago Galdston, M.D. 217 pages. D. Appleton-Century Company, New York, 1936.

³⁹*Syphilis and Its Treatment*. By William A. Hinton, M.D., Boston, Mass. 321 pages. The MacMillan Company, New York, 1936.

practically no reference is made to lesions of the disease in the female reproductive tract. The incidence of the disease in pregnant women is discussed from the racial angle. The primary lesion in the cervix is believed to be frequently overlooked or as frequently not recognized. The alcohol test (page 51) is not considered satisfactory in the female. The discussion of the infecting of married women by husbands early in the tertiary stage is of note in explaining the occurrence of syphilis, with no history of lesion or symptoms, in pregnant women.

The chapter on syphilis and marriage brings out clearly and significantly the position of the obstetrician or family physician in preventing social and reproductive tragedies. The advice given is concise and the author's conclusions are clinically sound. The chapter on congenital syphilis shows an estimated percentage of that condition in from 2 to 5 per cent of our population. The ideas of transmission are well established, the rules for preventing congenital syphilis are modern and effective, and the author feels that this proportion of syphilis could be almost entirely prevented. He recommends a routine Wassermann of every pregnant woman regardless of social status. Fortunately, this practice in clinic service is slowly but surely gaining in the United States. There is an excellent discussion of the signs, symptoms, and therapy of congenital syphilis. On page 275 under treatment of syphilis during pregnancy, caution is advised in the dosage of the heavy metals and arsenicals on account of the possibility of injury to the kidneys and liver.

This book should be read by the obstetrician, who in his work has the opportunity to promptly eliminate congenital syphilis, as well as to educate a large portion of the public in the campaign to eradicate the disease.

—Philip F. Williams

The second volume of *Postgraduate Surgery*,⁴⁰ edited by Rodney Maingot, contains more than 1,800 pages. The subjects covered include the head, spinal column, and salivary glands by Wakeley. The treatment of head injuries is very conservatively handled. An interesting chapter on cranial tumors is given. The advice that pituitary adenoma and carcinoma, if unaccompanied by papilledema, may be treated by radiotherapy is given. This entire part is illustrated with excellent x-ray photographs.

The neck is dealt with by Wheeler who uses either local, block, or rectal oil ether anesthesia. Avertin is not mentioned. The parathyroids are discussed very cursorily. No inclusion of scleroderma or Raynaud's disease is found. The breast by Love is much scantier in contrast to other important chapters. Both the anatomy and operative technic are barely touched upon. The important subject of the breast and its diseases deserves much more adequate treatment.

In contrast to this, the thorax is dealt with in considerable detail by two authors, Sleigh Johnson and T. Holmes Sellors. Johnson treats of postoperative chest complications and artificial pneumothorax. He discusses the medical aspects of chest troubles, including lung collapse, embolism, postoperative pneumonias, abscess of the lung for which he advises "bronchoscopic aspiration," cardiovascular complications, artificial pneumothorax. Much apparatus is described and illustrated.

The subject of surgery of the thorax is taken up by Sellors. This includes resection of the ribs for tuberculosis, phrenicectomy, empyema, both acute and chronic, but a description of the operation for pulmonary embolism is not included. The surgery of the chest concludes with tumors and bronchiectasis. This is very good.

The female genitals are described from various aspects. Regional Gynecology and Gynecological Operations are by J. Lyle Cameron. Apparently the watch spring rubber pessary is still used abroad. He emphasizes Schiller's test for carcinoma of

⁴⁰*Postgraduate Surgery*. Edited by Rodney Maingot, Senior Surgeon to the Royal Waterloo Hospital and to the Southend General Hospital, etc. Volume II. With 1,134 figures in the text, 3,572 pages. D. Appleton-Century Company, New York, 1936.

the cervix. No mention of lymphogranuloma inguinale is given, although esthiomène probably covers some of these cases. I am surprised to note that menopause flushes are treated by repeated venesection. Likewise, the injection of glycerin every two hours into a septic abortal uterus does not appeal to me. The same author likewise describes the gynecologic operations which are given in extenso. Sterility in women is dealt with by Forsdike. The major emphasis is placed on the mechanical aspects of sterility. Tumors of the ovary are described by Green-Armytage. This chapter is short and insufficient.

The urinary system and the male genital organs are covered by Ainsworth-Davis. The preliminary investigations and diagnosis are very well dealt with. The ketogenic diet is described in detail but more emphasis is placed on the acidification of the urine by mandelic acid. In the treatment of undescended testes, no mention of preputiary preparations is made.

An interesting chapter on the sympathetic nervous system by A. Lawrence Abel will be found. The anatomy of the abdominal sympathetic is very clear. There is a short but interesting exposition of this new field.

To me the most interesting and original contribution is on the adrenal gland by Broster and Vines. Broster, who describes the surgery, has 15 cases of virilism operated upon without a death, an amazingly good record. Vines offers a new test for determining the presence of the virilism factor in the adrenal by means of a Fuchsinophil stain (Ponceau fuchsin).

The next portion deals with injection treatment of hernia, hemorrhoids, hydrocele and varicocele, and varicose veins.

The concluding chapter by Buxton covers the subject of orthopedics.

Much of interest not only to the general profession but also to surgeons will be found in these pages.

—R. T. Frank

Pincus' *The Eggs of Mammals*⁴¹ is a most interesting and stimulating short monograph. It deals with the behavior of the mammalian egg from its genesis in the ovary to its implantation in the uterus. The author does not believe that the definitive ova of adult life arise from the primordial germ cells. On the contrary, he favors the view that the mammalian ova have a short life with a periodic production of new ova, the rate of their proliferation varying with the various stages of estrus and pregnancy cycles. The determining factor, according to Pincus, is the pituitary secretion which inhibits follicular changes, favoring maturation of the ova.

He considers regeneration of ovogenetic tissue improbable in mammals, based on the work of Parkes, but concedes the regeneration of anovular follicles after x-ray destruction of the existing ova. These anovular follicles are capable of producing ovarian hormones.

While the reviewer realizes that in such pioneer studies some evidence though hypothetical must be considered, he cannot agree with the view expressed that granted that pituitary secretions are concerned with the promotion of ovulation and luteinization they presumably inhibit ovogenesis to a certain extent; nor that the thyroid may promote ovogenesis directly. The facts at present available are far too slender to warrant any definitive judgment. This applies as well to hypothetical atresia suppressing hormone.

This monograph is very well worth reading. It is the first of a series of experimental biology monographs of which 14 others are already announced.

—R. T. Frank

⁴¹*The Eggs of Mammals.* By Gregory Pincus, Assistant Professor of General Physiology, Harvard University. 160 pages, illustrated. The MacMillan Company, New York, 1936.

This volume, the seventh in *Les Problèmes D'Oncologie*,⁴² is dedicated to the memory of M. I. Lifshitz. It is written in Russian but, fortunately for the reviewer, a majority of articles have summaries in French and English. While the English is somewhat quaint, it is understandable.

The 19 articles are by numerous authors. One group deals with gastritis and its relation to carcinoma. Another group describes the effect of "prolan" upon the growth of experimental cancer. The final group concerns itself with clinical cancer, including that of the skin which appears to be extremely prevalent on exposed parts in the Ukrain. Radiotherapeutic measures for combating clinical cancer are discussed.

—R. T. Frank

Volume I, Part 2, of *The Patient and the Weather*,⁴³ contains 781 pages, with innumerable graphs, maps and illustrations. The first volume was devoted to the graphic distribution of diseases in the United States, with the inference that meteorologic environment had much to do with the reaction of the human organism. According to the author, medicine has concentrated too much on infectious diseases. He quotes Haldane as saying that we must direct our views from microorganisms to the patient. This will imply closer study of the environment. The constitution of the patient should take into consideration the limitations of biological reactions as regulated by the autonomic nervous system and as influenced by the meteorological environment, in normal individuals to start with, including chemical, endocrine and nervous factors. The organism swings in a definite rhythm, increasing and decreasing as far as its oxidation, its pH, metabolism, blood pressure, etc., are concerned. The peaks and drops are both of clinical significance. Even the possible changes of the human organism in response to the ordinary common meteorological changes have been studied. A wealth of clinical detail and statistics are included. This book will appeal to the statistically minded because of the huge amount of data and documentation.

—R. T. Frank

Cobb's *Preface to Nervous Disease*⁴⁴ is based on fourteen years' teaching of second-year students in neuropathology. To quote the author's own words, it is "a brief, concurrent anatomy, physiology, and pathology." In a short compass of 173 pages, this large task is attained by means of careful selection and compression. Simple but well-executed diagrams as well as a short bibliography at the end of each chapter add to the value of this manual.

—R. T. Frank

*Food, Fitness and Figure*⁴⁵ is a story of our sources of strength and health written for the intelligent public. The subject is one of universal interest, and the facts presented are not only correct but are given in a very pleasing manner. The structure of the dietary elements, their basic components, the sources and need for iodine, calcium, the vitamins and the beverages, the constituents of a normal diet

⁴²*Les Problèmes D'Oncologie*. Tome VII. édition Médicale d'État D'Ukraine, 1935. (In Russian.)

⁴³*The Patient and the Weather*. By William F. Peterson, M.D. Volume I, Part 2. Automatic Integration. Illustrated, 781 pages. Edwards Brothers, Inc., Ann Arbor, Mich., 1936.

⁴⁴*A Preface to Nervous Disease*. By Stanley Cobb, M.D., Bullard Professor of Neuropathology, Harvard Medical School, etc. 173 pages. William Wood & Company, Baltimore, 1936.

⁴⁵*Food, Fitness and Figure*. By Jacob Buckstein, M.D., Consulting Physician in Diseases of Stomach and Intestines, United States Veteran Bureau, etc. 252 pages. Emerson Books, Inc., New York City, 1936.

and their balancing, form an interesting story well calculated to be understood and appreciated by the layman. Such dietary aberrancies as vegetarianism and fasting are discussed.

The problem of weight control is simply and clearly explained, and the patent medicine fakes and ballyhooed diets debunked. Three well-constructed diets, for a fortnightly period to lose, maintain or gain weight are detailed. The statement is made that weight loss should at no time exceed two pounds a week. There are included standard 100 calorie tables and percentage element food source graphs. The book may be warmly recommended to the public.

—Philip F. Williams

Dr. Logan Clendening, author of several books on medical subjects written essentially for the laity, now turns to food. His latest is *The Balanced Diet*.⁴⁶ In it the author in his well-known clear, interesting style presents a discussion of the constituents of foods as well as diet in health and disease from a middle-of-the-road point of view. There is also a commendable attack upon food faddism, and here he writes energetically and with malice aforethought.

Regardless of what one's opinion may be as to the propriety or advisability of the dissemination of medical literature to the general public by physicians, it must be admitted that this book will be extremely valuable not only to the laity but also to physicians. Since the written is always so much more efficacious than the spoken word, it may help the latter in perhaps eliminating some of the skepticism that patients not infrequently manifest when certain healthful but obnoxious diets are prescribed.

Numerous tables and illustrations showing the constituents of the common foods as well as their caloric value are also presented.

—Frank Spielman

This widely used dictionary⁴⁷ with the appearance of this new, revised edition celebrates its twenty-fifth anniversary. It reflects the latest revisions of the U. S. Pharmacopoeia and the National Formulary with the addition and elimination of many drugs, and changes more recently adopted in chemists' spelling. The elimination of required instruction in Latin and Greek by many American colleges made it desirable to include a short chapter on medical etymology, dealing with medical orthography and the common prefixes and suffixes, Latin and Greek, used in medical nomenclature. There also is added a list of English terms which by the Anatomical Society of Great Britain and Ireland have been suggested to replace in part the official Basle Anatomical Nomenclature.

—Hugo Ehrenfest

*Boy or Girl*⁴⁸ by Dr. Jules Regnault, who according to the title is ex-professor of anatomy at the Naval Medical School, is a farrago of nonsense based particularly on the defunct Albert Abrams' method. Regnault also presided at a conference of "radiotellurists and sorcerers." In his biography, supposedly written by the editors, it mentions that he operated upon himself under local anesthesia for hernia. According to the text, women can have the choice of girls or boys to suit themselves, if they follow the directions given by the author.

—R. T. Frank

⁴⁶*The Balanced Diet*. By Logan Clendening, M.D., Professor of Clinical Medicine, University of Kansas. Illustrated, 207 pages. D. Appleton-Century Co., New York, 1936.

⁴⁷*Medical Dictionary*. By Thomas Lathrop Stedman, A.M., M.D. Thirteenth revised edition. Illustrated, 1,291 pages. William Wood and Company, Baltimore, 1936.

⁴⁸*Fille ou Garçon*. Par Docteur Jules Regnault. Editions Medica, Paris, 1936.

Department of Reviews and Abstracts

CONDUCTED BY HUGO EHRENFEST, M.D.

Selected Abstracts

Carcinoma

Reimers, Carl: Results With the Klein Carcinoma Reaction, München. med. Wehnschr. 83: 1375, 1936.

Reimers reports on the Klein reaction in 691 blood tests made on as many patients. Of these, 438 cases were definitely diagnosed clinically and histologically as follows: (a) 38 cases of malignant tumors (not skin carcinomata) with the Klein reaction positive in 32 and negative in 6, a correct average in 84.3 per cent; (b) 28 cases of benign tumors giving a positive Klein in 2 cases and negative in 26 cases, a correct average in 92.9 per cent; (c) 372 cases that were cancer-free with a positive Klein in 19 cases and a negative reaction in 353 cases, a correct average in 95 per cent. Among the 691 cases there were also 24 which had not been completely studied when the Klein reaction was made, but in which finally the reaction was determined to be correct in 23 instances and false in 1, a correct average of 96 per cent. There were also 172 cases in which certain factors, such as preceding x-ray and radium treatments, operations, medications, hemorrhages, etc., might be considered as interfering with the proper interpretation of the Klein reaction, a fact to which Klein himself has called attention. Of these 172 cases there were (a) 42 cases with malignant tumors in which the results were correct in 33.4 per cent and false in 66.6 per cent; (b) 130 cases which included those that had benign tumors and also those that were tumor-free in which the results were correct in 70 per cent and false in 30 per cent. The remaining 57 cases were not available for complete and final diagnoses. Although the percentage of correct results was slightly higher in the nonmalignant cases, the malignant conditions seemingly can be diagnosed with a certainty in about 90 per cent of cases.

C. E. PROSHEK.

Grögler, Fritz: Experience With the Klein Carcinoma Reaction, München. med. Wehnschr. 83: 1377, 1936.

Grögler summarizes his results with the Klein carcinoma reaction in 90 clinic cases, suspected of having malignant tumors. There were available for exact study 68 cases in whom there were no disturbing or complicating factors. In 92.6 per cent of these the Klein reaction proved to be correct. This corresponds with the findings of other clinics.

C. E. PROSHEK.

Hendriksen, Erle: Precancerous and Carcinoid Lesions of the Cervix Uteri With Comments on the Schiller Test, Surg. Gynec. Obst. 60: 635, 1935.

In the great majority of cases, the diagnosis of carcinoma is simple, either clinically or pathologically, and microscopic examination is only confirmatory. The

microscopic diagnosis of cervical cancer will not be improved until both the clinician and the pathologist learn more about pseudomalignant and possible premalignant lesions of the cervix.

Mitotic figures are occasionally seen in the basal layer of the normal cervical epithelium and are to be looked upon as evidence of the normal growth and repair of the cervix.

Cervical lesions may be spoken of as "precancerous" when it is understood that the term implies that they might, though not necessarily will, become cancerous.

Leucoplakia of the cervix is a pathologic entity which may show cellular changes suggestive of cancer, though invasion is always lacking.

An interesting case is described of intracervical carcinoma, diagnosed with the aid of the Schiller test, and in which the malignant growth extended over the entire endometrial surface of the uterus.

The importance of biopsy is indisputable, but its value is increased if the specimen is immediately fixed and serial sections are made.

The application of Lugol's solution with the atomizer simplifies the Schiller test which is undoubtedly of some value in the diagnosis of early cancer; whether it is a specific test for the absence of cancer is questionable.

WM. C. HENSKE.

Wetterdal, P.: Does the Microscopic Diagnosis Afford a Prognostic Guide in Cervical Cancer? A*ta obst. et gynec. Scandinav. 14: 302, 1934.

In the Radium Home at Stockholm a study was made of 354 cases of cervical cancer to determine the relationship between the histologic appearance of the cancer and the results obtained with radium treatment. Clinically the cases were divided into the four groups proposed by the Cancer Commission of the League of Nations and the cases were followed for at least five years. The percentage of cures for the different groups was so nearly identical that the author believes it safe to assume that the microscopic appearance of the cancer is of no prognostic significance. Kamniker came to the same conclusion from an analysis of cases studied microscopically and treated either by operation alone or by combined operation and radiation therapy.

J. P. GREENHILL.

Feldwig: The Relation Between the Histology, the Prognosis, and the Therapy of Genital Carcinoma, Ztschr. f. Geburtsh. u. Gynäk. 111: 1, 1935.

Feldwig studied 422 cases of cancer of the uterus, vagina, and vulva histologically. He divided the cases into four grades: ripe, middle ripe, unripe and structureless. He found adenocarcinoma and squamous cell cancer present in the same lesion in 2.1 per cent of all the cases. The ratio of squamous cancer to adenocarcinoma of the cervix was about 10 to 1; and the same ratio, but reversed, applies to cancer of the fundus of the uterus. He found that the maturity of the cancer cell increases with the age of the patient. There are differences in radiosensitivity in the various grades of cancer, but an absolute radioresistance does not exist. Adenocarcinoma of the cervix was found to be more resistant to radiation than was squamous cancer. Fractional irradiation produces the best results in cancers of the middle ripe group regardless of location or cell differentiation. A moderate number of mitoses and a moderate degree of hornification as well as a cellular reaction (lymphocytes, leucocytes or eosinophiles) indicate the most favorable prognosis from irradiation. Surgical results were slightly better in the cases of low maturity than those with more advanced maturity. (The reviewer does not believe that the author's figures for adenocarcinoma-squamous cancer ratio

in the fundus of the uterus can be accepted, nor that his statements on the comparative radiosensitivity of adenocarcinoma could be substantiated by workers in this country.)

EUGENE S. AUER.

Norris, Charles C.: Adenocarcinoma of the Cervix, Am. J. Cancer 27: 653, 1936.

A compilation of 9,505 cases of cervical cancer reported in literature shows an incidence of 5.7 per cent for adenocarcinoma of the cervix, a relatively small percentage. Analyzing 43 cases seen in the gynecologic service of the Hospital of the University of Pennsylvania, Norris arrives among others at the following conclusions: Adenocarcinoma of the cervix presents many different histologic types. It seems that the embryonal (unripe) tumors are about twice as fatal as the ripe or adenoma malignum neoplasms. In general the proportion of cells undergoing mitosis offers a fairly accurate guide as to the degree of malignancy and radiosensitivity. Adenocarcinomas are more prone to develop in the cervical canal and in this situation the first symptoms appear later which means it often is rather far advanced when diagnosed. As a group they are not less sensitive to irradiation than the epitheliomas of the same region.

HUGO EHRENFEST.

Overholser, Milton D., and Allen, Edgar: Atypical Growth Induced in Cervical Epithelium of the Monkey by Prolonged Injections of Ovarian Hormone Combined With Chronic Trauma, Surg. Gynec. Obst. 60: 129, 1935.

The ovarian follicular hormone has been shown by Allen and many others to be a powerful stimulator of epithelial growth in the female genital tract and breast.

Atypical epithelial growth in the cervix uteri of 4 ovariectomized monkeys (Monkeys 1 to 4) was experimentally produced. The changes consisted of marked squamous epithelial downgrowth, overgrowth, and epidermization of the cervical glands in the region of the junction of the stratified squamous with the columnar epithelium. The treatment these animals received was as follows:

Monkey 1 received 5,490 R.U. of estrin in ninety days, with repeated cervical trauma.

Monkey 2 received 1,660 R.U. of estrin in twenty days, with repeated cervical trauma.

Monkey 3 received 4,747.5 R.U. of estrin and 14 c.c. of corpus luteum extract in 81 days with repeated cervical trauma.

Monkey 4 received 2,802.5 R.U. of estrin and 10.7 c.c. of corpus luteum extract in eighty-four days. This animal did not receive cervical trauma and the changes were very pronounced, the epithelial cells being very atypical.

In three other monkeys the results were practically negative possibly due to the following reasons: (1) injection period too short (Monkey 5); (2) sloughing of epithelium from severe infection (Monkey 6); (3) sloughing of epithelium from infection and from stopping hormone injections forty-two days before sacrificing animal. (Monkey 7.)

A normal control (Monkey 8) receiving trauma only showed a slight amount of epidermization of cervical glands.

An ovariectomized control (Monkey 9) receiving trauma only was completely negative.

It should be possible by repeating these experiments and extending them over much longer periods of time to determine experimentally whether the changes in question will or will not develop into cancer in the monkey. Either result would be highly important and experiments are now being carried out with a view to

demonstrating this point. To what extent the various experimental factors such as trauma, estrin, and corporin, respectively, are responsible for the results obtained also needs further analysis.

WM. C. HENSKE.

Crossen, R. J., and Hobbs, J. E.: Relationship of Late Menstruation to Carcinoma of the Corpus Uteri, J. Missouri M. A. 32: 361, 1935.

The incidence of late menopause in cases of adenocarcinoma of the fundus uteri is about four times as high as it is in normal cases. In this series, a study of the slides of previous curettages done in fundal carcinoma cases indicates that endometrial hyperplasia is an important predisposing factor in adenocarcinoma of the fundus. A study of such slides whenever possible will help to settle definitely the question of the importance of endometrial hyperplasia as an etiologic factor in fundal cancer. Late menopause, especially when extending to the age of fifty, is a warning of a tendency to endometrial malignancy, and adequate treatment should be given to stop the aberrant endometrial activity.

J. THORNWELL WITHERSPOON.

Wittenbourg and Zlatmann: Post-Climacteric Hemorrhages and Their Relation to Malignant Neoplasms, Rev. franç. de gynéc. et d'obst. 30: 1026, 1935.

The authors collected 100 personal cases of postclimacteric bleeding among which 41 per cent had malignant growths causing the bleeding. They collected from literature 2,384 reports of postclimacteric bleeding. In this series the incidence of malignancy was 62.8 per cent. Other causes were benign neoplasms in 4.5 per cent, inflammatory disease in 20.3 per cent, urinary tract affliction in 0.6 per cent, diverse causes in 6.9 per cent, and unknown causes in 4.9 per cent.

Some gynecologists objecting to exploratory curettement, in cases of post-climacteric bleeding perform a hysterectomy on the clinical symptoms alone. The present authors are not of this opinion because otherwise they would have performed unnecessary operations on a large proportion of their patients. Since most of these women are old and in poor physical condition, there is a high operative mortality for hysterectomies.

J. P. GREENHILL.

Henriksen, Erle: Carcinoma of the Cervix Uteri, Arch. Surg. 31: 461, 1935.

From a clinical study of 940 cases of cervical cancer the author draws conclusions among which the following seem noteworthy: The average age of these patients was forty-six years, with cancer occurring in 66.3 per cent before the age of fifty years. Over 10 per cent were never pregnant. Postcoital spotting occurred in less than 5 per cent. In 50 per cent there was some involvement of the urinary tract, mostly nocturia. Loss of weight or pain has no diagnostic value. The possible influence of heredity is still a disputed question. Among the 940 cases were 22 in which the cancer developed in a cervical stump after subtotal hysterectomy with an average lapse of five years.

HUGO EHRENFEST.

Ulrich, P.: Cancer of the Cervix. The Etiologic Rôle of Previous Surgical Traumatism, Compt. rend. Soc. franç. de gynéc. 6: 238, 1936.

In the opinion of the author it is an established fact that the traumatism of labor plays an important rôle in the etiology of cancer of the cervix. However, this form of injury does not exist as a forerunner of cervical carcinoma in nullip-

arous women. In these cases, the author believes, mechanical damage inflicted by surgical instruments is an important factor. Especially dangerous are the *Museux* forceps which have damaging prongs with which the cervix is grasped. The sharp pointed teeth of this clamp carry healthy epithelium into the depths of the cervix and here under certain conditions the cells become transformed into cancer. Because of this, the author has had constructed a special form of this instrument which he believes cannot injure the cervix.

J. P. GREENHILL.

Döderlein, G.: Cancer of the Cervix in Young Women, Ztschr. f. Geburtsh. u. Gynäk. 110: 349, 1935.

In the author's clinic 48 women under thirty years of age were found with cancer of the cervix, i.e., 5.15 per cent of all cervical cancer cases seen. In 44 of the 48 cases a period of but four months or less had elapsed since the onset of the first symptoms. The operability rate was 92 per cent, an unusually high figure for any series of cancer cases. The 48 cases were treated as follows: 41 with Wertheim operation; 2 with Wertheim operation preceded by radiation; 1 with Schauta operation; 4 with radiation therapy only. There was a total five-year cure rate of 48 per cent (absolute), and a five-year cure rate of 52.3 per cent in the operable cases. Döderlein concludes from a study of these cases that there is no reason for the prevalent pessimism in the prognosis of the disease in young women, if the diagnosis is made at the proper time and proper therapeutic measures are instituted. There is no difference in the response of younger patients to operation, radiation or a combination of the two, than in the older woman. The results should be about the same, if not better, in the younger woman because her physical condition, as a rule, will be better. He believes that every young woman treated by a radical operation should have a transplantation of a healthy ovary into the rectus sheath.

EUGENE S. AUER.

Tompkins, Pendleton: Statistical Study of the Relation of Parity to Carcinoma of the Cervix Uteri, Am. J. Cancer 25: 624, 1935.

It is doubtful whether the relation between parity and cervical cancer can be reliably determined from the statistics at present available. However, from computations based upon such data as could be secured, it appears that in the United States in 1930, among women thirty years of age or over, the death rate from cervical carcinoma was at least twice as great among those who had borne children as among those who had not.

HUGO EHRENFEST.

Stout, T. D. M.: Cancer of the Cervix Uteri, New Zealand M. J. 34: 97, 1935.

Conditions arising in the cervix following parturition and their relationship to cancer are discussed. Two generally accepted precursors of cancer are trauma and sepsis. Erosion and chronic cervicitis, in view of their prolonged infective nature and chronicity, are opposed as causative factors by some and held responsible by others as possible precursors of cancer.

The author concludes from various records that trauma alone is not responsible for the development of cancer. The weight of evidence points to the theory of cancer's being due to chronic infective processes. Leucoplakia is definitely a precancerous lesion.

Early diagnosis and prevention are discussed in detail. Biopsy is advocated for diagnosis and treatment of chronic infections of the cervix as a means of

prevention. Because of the large incidence of cervical cancer following subtotal hysterectomy in multiparas, the author reserves this operation for single women only.

F. L. ADAIR AND S. A. PEARL.

Reckmann, R.: Sarcoma of the Cervical Stump, Arch. f. Gynäk. 155: 478, 1936.

The author reports the occurrence of a spindle-cell sarcoma in a cervical stump. A necrotic submucous fibroid the size of a fetal head had been removed together with the uterus by means of a supravaginal hysterectomy, and seven months later a necrotic tumor of the cervix as large as the primary tumor of the uterus was found in the cervical stump and protruding into the vagina. This was removed and the patient was given intensive irradiation in spite of the fact that the tumor resembled benign fibromyoma when examined microscopically. Six weeks later there was a fist-sized recurrence which was found to be a typical spindle-cell sarcoma. The author is of the opinion that the primary tumor was sarcomatous as well.

RALPH A. REIS.

Fahndrich, Joachim: The Risk of Carcinoma of the Cervix Following Supravaginal Hysterectomy, Ztschr. f. Geburtsh. u. Gynäk. 109: 382, 1934.

The author reports 12 cases of cervical stump cancer treated in the Kiel clinic between 1922 and 1933. A fairly complete compilation of the world statistics concerning stump cancer and its relation to supravaginal hysterectomy is presented. Several theories about the etiology of this type of cancer are mentioned, mostly discarded as probably erroneous. The only definite factor is that the condition is seen far oftener in the multipara than in the primipara or virgin. The author believes that cancer may develop at any time after the original operation, but the first year is the most dangerous. The incidence of cervical stump cancer in the Kiel clinic was 0.28 per cent when compared with the number of supravaginal operations done; the figure is 0.39 per cent in the accumulated statistics of literature. Regardless of prophylactic precautions such as coring out the cervical canal, or cauterization with the actual cautery or phenol, or the careful discrimination in choosing patients for this operation, a certain small percentage of cancers will develop in the stump. At first glance this would tend to make the argument in favor of the complete removal of the uterus and cervix overwhelming. However, the author then makes an extensive study of the mortality figures in the various large clinics of the world, comparing the figures for the complete operation with those of the supravaginal operation, and finds that in uncomplicated cases there is a minimum difference of 1.75 per cent in favor of the supravaginal operation. This figure increases materially in the face of complications of more extended operations. It therefore follows that even if all the patients developing stump cancer would die from that disease, the mortality of the supravaginal hysterectomy would still be materially less than the mortality from abdominal total extirpation of the uterus.

EUGENE S. AUER.

Séjournet, P.: Cancer of the Cervix After Subtotal Hysterectomy, Bull. soc. d'obst. et de gynéc. 24: 278, 1935.

The author reports two cases of cancer of the cervix after subtotal hysterectomy. In a study of the literature he found a total of 387 cases published up to 1935. Up to 1926 there were reports of only 85 such cases but from 1926 to 1935, 302 additional cases have been added. The author obtained his statistics from two

sources, namely, Surgical Services and Anti-Cancer Clinics. The cases covered by the Surgical Services were small in number compared with the large series reported by the Anti-cancer Clinics. From large series of cases reported by surgeons the incidence of cancer of the cervix after hysterectomy was 2.19 per cent, whereas in the series reported by cancer clinics the incidence of late cervical cancer was 4.17 per cent. The author collected 9 instances of cancer which developed in the vaginal scar. He discusses the treatment of late cancer of the cervix.

J. P. GREENHILL.

Barthélemy: Cancerization of Fibroids, Bull. Soc. d'obst. et de gynéc. 25: 164, 1936.

The author points out that three signs indicate a cancerous change in a fibroid. These are in the order of their frequency: pain, a foul discharge, and emaciation. The pain is continuous, in the pelvic region, with attacks of exacerbation and radiation to the lumbar region and the thighs. The vaginal discharge is liquid, thin and foul smelling. A woman who has uterine fibroids may be anemic and weak from loss of blood, but she does not become emaciated. However, when the fibroid becomes cancerous, the woman becomes cachectic.

The author collected from the literature 34 cases of fibroids which underwent cancerous change. In this collected series 23 complained of pain, 14 mentioned that they had a foul discharge and 9 showed emaciation.

It is important to make a diagnosis of cancerous change of a fibroid because if radiation therapy is employed without this knowledge, the favorable time for a total hysterectomy has passed. This is essential because this operation is the only rational treatment for cancerous change of a fibroid.

J. P. GREENHILL.

Fournier, R.: Cancer of the Body of the Uterus After Irradiation for Metrorrhagia, Bull. Soc. d'obst. et de gynéc. 24: 309, 1935.

The author reports a case where cancer occurred in the body of the uterus after the patient had received x-ray therapy for metrorrhagia. In the literature, particularly German, he found 65 cases of uterine cancer after radiotherapy for benign gynecologic conditions. The interval of time between radiation and appearance of the cancer varied from two months to ten years. The author does not believe there is any justification to admit a causal relationship either direct or indirect. An irradiated uterus is not predisposed to cancerous changes.

In half of the published cases it was doubtful whether the original condition for which the radiation therapy was used actually was benign. It is more probable that the cancer existed before the treatment with x-rays. The author emphasizes that in every case of uterine bleeding before radiotherapy is used a curettement should be performed, and all material examined microscopically. In some cases intrauterine injection of lipiodol may be used or a biopsy of the cervix made.

J. P. GREENHILL.

Dickinson, Arthur M.: Modern Treatment of Carcinoma of Uterus, Am. J. Surg. 32: 395, 1936.

Carcinoma of the uterine cervix is usually of the epidermoid type. Accurate histologic diagnosis by biopsy is essential; biopsy risk is very slight. Cervical carcinoma is best treated by a combination radium and deep x-ray therapy. By the use of the deep therapy before radium application the danger of fatal peritonitis is minimized. Surgical treatment has proved inadequate in comparison with radiotherapy.

Carcinoma of the uterine corpus is usually of the glandular type. Diagnosis can generally be made by a curettage but cancer should be suspected in patients who commence to have a discharge or bleeding after the menopause. Carcinoma of the body is best treated by a course of deep x-ray therapy followed promptly by a panhysterectomy.

J. THORNWELL WITHERSPOON.

Malpas, P.: Corporeal Recurrence After Radium Treatment of Carcinoma Cervicis, Lancet 2: 1464, 1935.

There were 5 cases in 359 cervical carcinomas that had corporeal recurrences after radium therapy. The symptoms of the recurrences were irregular lower abdominal and lumbar pain and a return of the watery discharge. The uterus enlarged and became globular. Extension to the ureters and bowel are common complications. It is emphasized that hysterectomy has no place in the secondary treatment of cervical carcinoma for at least twelve months after radium treatment and that the uterine applicator be sufficiently long for treatment.

H. CLOSE HESSELTINE.

Mackenzie, Kenneth: Advanced Cancer of the Cervix Treated With Acetone and X-Radiation, New Zealand M. J. 35: 309, 1936.

Two cases of squamous cell epithelioma of the cervix in an advanced stage were treated by the application of pure acetone followed by x-ray irradiation. A marked improvement in the symptoms occurred immediately following this treatment and ultimately the ulcerating lesions which filled the vaginal vault completely disappeared. One year later both patients appeared free from the disease.

One other case treated similarly by the author resulted in only temporary alleviation of the discharge.

F. L. ADAIR AND S. A. PEARL.

Mackenzie, Bruce: Radiotherapy of Cancer of the Cervix Uteri, New Zealand M. J. 34: 171, 1935.

Radiologic treatment of cancer involves a distinction between two factors: alleviation or cure. Alleviation is obtained upon incomplete eradication of cancer cells. This applies to advanced, widespread, hopeless cases. Cure comprises complete eradication of all malignant cells and their conversion into benign tissue. The author deals with this group particularly.

Fundamentally, an adequate dose to all cancer cells and a regulated dose that will cause no damage to normal surrounding tissues are essentials.

There is no fixed lethal cancer dose. Some radiosensitive cancers may be eradicated by a dose of 1,000 r., while radioresistant types may not be cured by 10,000 r. Between these extremes lie many gradations. The percentage of cures increases with increasing dosage. Damage to normal tissues must be avoided. Normal tissue tolerance varies with different tissues. In gynecologic work 3,000 to 4,000 r. tissue dose may be safely given in the course of a month. A homogeneous distribution of dosage through the entire tumor area is essential. X-ray may be used beneficially in conjunction with radium. Methods of x-ray treatment and their sequelae and complications are described. Local reactions, diarrhea, cystitis, vaginitis, and amenorrhea with sterility commonly follow, and all but the last require treatment.

The author feels that where no reactions occurred an inadequate dose was administered. The larger doses, though drastic, give the best results. Early treatment is most important from the radiologic aspect because (1) the area involved is smaller, and (2) young tumor cells are more vulnerable than old ones.

F. L. ADAIR AND S. A. PEARL.

Carranza, Felipe F.: A Consideration of the Treatment of Carcinoma of the Vulva, *Boll. de Soc. de ostet. y ginec. (Buenos Aires)* 15: 369, 1936.

After reviewing his cases and results obtained by the several methods employed the author arrives at the following conclusions:

The treatment of choice in carcinoma of the vulva is electrosurgery not only of the local area, but also of the areas of regional metastasis, and extirpation of the lymph glands, four to six weeks following the vulvectomy. During the interval deep x-ray therapy is applied over these areas.

The technique of treatment varies with the extent of involvement. Simple vulvectomy suffices in very early cases. In them, if the initial lesion is small, radium may be employed. In lesions of the second and third grade electrosurgery with electrocoagulation of all regional lymph glands must be employed.

It is best not to close the denuded areas with sutures but permit them to granulate.

MARIO A. CASTALLO.

Salacz, Paul von: The Surgical Treatment of Cancer of the Female Genitalia, *Ztschr. f. Geburtsh. u. Gynäk.* 110: 290, 1935.

Operable cancer of the cervix is best treated by a combination of radiation and radical surgery which gives 18 per cent better results than either method alone. In the II. University Clinic of Budapest the radical vaginal operation (Schauta) is used rather than the abdominal operation of Wertheim because the final results are about the same, while the primary mortality, postoperative morbidity and complications are much greater with the abdominal operation. Inoperable cancer, as well as operable cancer complicated by old age, diabetes, hyperthyroidism, cardiorenal disease, etc., is treated only by radiation. Over a period of seventeen years, 217 cases of cervical cancer were operated by the Schauta method. Primary mortality was 3.6 per cent and morbidity 7.7 per cent. Uneventful recovery without a rise in temperature occurred in 55 per cent. There were 46.5 per cent of five-year cures. Pregnancy complicated by cancer of the cervix does not have the extremely bad prognosis generally believed. Cancer in pregnancy is treated by radical methods, either with or without cesarean section, depending upon the period of gestation and the extent of the cancer at the time that it is discovered. In his clinic the results were about the same as with cancer not complicated by pregnancy. Cancer of the uterine body is best treated by vaginal hysterectomy. The five-year cure rate in 81 cases was 73 per cent. Cancer of the vulva was treated by radiation, although the author describes the correct surgical procedure. No end-results are greater, but the prognosis is given as very bad. A few cases of cancer of the vagina were treated surgically with the results extremely unsatisfactory. Two cases of primary cancer of the tubes were seen. The patients lived less than one year after operation. Three cases of Krukenberg tumor are reported. Regardless of the age of the patients all ovarian tumors should be operated as soon as possible. Of 130 cases operated more than five years ago 36.9 per cent are living and well. Inoperable cancers of the ovaries are treated by radiation, but the results are universally bad.

EUGENE S. AUER.

Auer, E. S.: Carcinoma of the Cervix, J. Missouri M. A. 32: 47, 1935.

Auer analyzes 136 cases of cancer of the cervix treated at a St. Louis Cancer Hospital from January, 1927, to January, 1930. Twenty-nine or 21.3 per cent were cured. A complete follow-up was obtained on all patients. The cervical malignancies were grouped according to the classification of the American College of Surgeons.

Auer believes that the radical operation, either by vaginal or abdominal route, has a very definite place in the treatment of cervical cancer, provided its use be reserved for those patients in whom there is absolutely no extension of the disease laterally. Radiation, combined with conservative surgery, is the method of choice in borderline cases. A watchful waiting policy should never be adopted in suspicious cervical lesions. Radium treatment of this disease should be carried out only by those who are qualified.

J. THORNWELL WITHERSPOON.

Greenhill, J. P., and Schmitz, Herbert: Intraspinal (Subarachnoid) Injections of Alcohol for Pain Associated With Malignant Conditions of the Female Genitalia, J. A. M. A. 105: 406, 1936.

Twenty-seven subarachnoid injections of alcohol in 25 women suffering excruciating and persistent pain from advanced carcinoma of the genitalia were made. Relief lasting from two weeks to six months was attained in 24 out of 25 patients. For 21 of the injections 0.5 c.c. of 95 per cent alcohol was used and injected into the fourth lumbar interspace. The technic varies only slightly from that of the lumbar puncture and is surely much simpler than any operative procedure such as sympathectomy which the writers had recommended for the same purpose two years ago.

GROVER LIESE.

Organotherapy

Neumann, H. O.: Treatment With Female Sex Hormones, Med. Klin. 32: 79, 1936.

The author treated many women with female sex hormones for a number of different gynecologic ailments. The results in cases of primary amenorrhea were not satisfactory. In secondary amenorrhea the author obtained encouraging results with a combination of estrogenic hormones and progestin. The patients felt much better physically and mentally. However, in the prolonged cases of secondary amenorrhea, the results were not satisfactory. In many cases with weak and infrequent menstrual periods, favorable results were obtained with estrogenic substance. In cases of hypoplasia of the uterus there was a growth of both the body of the uterus and the endometrium. In seven cases of dysmenorrhea the pain was relieved by follicular hormones. Treatment in these cases had to be continued at least six months. Likewise benefit was observed in women with severe menopausal symptoms. The author was also able to help some women with ulcerations in the vagina and vulva and pruritus vulvae. Using corpus luteum hormone he was able to bring to a successful issue two cases of habitual abortion.

J. P. GREENHILL.

Westman, A.: Hormonal Therapy for Menstrual Disturbances and the Theoretic Reasons for It, Acta obst. et gynec. Scandinav. 15: 233, 1935.

In the Upsala Clinic, a number of women with menstrual disturbances were treated with various hormones. In two out of three cases of primary amenorrhea, favorable results were obtained with prolactin and estrogenic substance. In 17 cases

of secondary amenorrhea the following results were observed: No success in three cases treated with prolan. One good result in 4 treated with estrogenic substance given hypodermically. Among 5 cases of secondary amenorrhea, treated by a combination of prolan and estrogenic substance, there were 2 successes and 3 failures. In 3 cases of puberty bleeding, prolan produced considerable improvement in one case and partial help in two other instances. Among 8 women with menopausal bleeding treated with corpus luteum hormone only 3 showed good results. For climacteric disturbances, estrogenic substance administered by mouth proved helpful.

J. P. GREENHILL.

Fairlie, Margaret: Ovarian and Pituitary Hormones, Brit. M. J. 2: 533, 1935.

A hypoplastic uterus may be induced to grow and develop to normal size by estrin. During pregnancy estrin and the mechanical stimulus of the placenta ensure progressive growth of the uterus. The estrin level in the blood rises from time of rupture of follicle until menstruation, which is accompanied by a sudden drop. In the urine estrin is excreted during the normal menstrual cycle in amounts from 1,200 to 2,000 M.U. During pregnancy it is excreted in amounts over 50,000 M.U. in twenty-four hours. It has been suggested that the placenta produces a large part of it during pregnancy.

Progestin acts on the uterine endometrium only after it has been sensitized by estrin. If pregnancy occurs, progestin is responsible for the formation of the decidua, and the arrest of the ripening of fresh follicles. The periodicity and rhythm prevailing in uterus and ovary throughout normal sexual life are obviously under the control of the anterior pituitary gland.

In castrated animals, castration cells appear in the anterior pituitary; these may disappear on the administration of estrin and reappear on withdrawal. Thus the interrelationship of the pituitary and ovary are observed, i.e., the anterior pituitary stimulates the production of estrin, and the estrin affects the anterior lobe.

The question is yet unanswered as to what is responsible for the rupture of the graafian follicle and ovulation. It is claimed that there is a sudden rise in prolan A in the urine in the mid-menstrual cycle, which may be the stimulus to ovulation.

Metropathia hemorrhagica is an entity characterized by amenorrhea of some weeks' duration, followed by hemorrhage lasting for weeks. It is associated with multiple follicular cysts and represents an anovular menstruation. No corpus luteum is present. The endometrium is hyperplastic, containing dilated, cystic glands, and areas of necrosis in the superficial layers of the membrane. Estrin is credited as the source of the marked hyperplasia of the endometrium during the period of amenorrhea. Administration of estrin is, therefore, contraindicated in this form of uterine bleeding. Curettage is advisable for diagnosis and the removal of thickened endometrium gives relief in some cases. Corpus luteum hormone (prolution) is giving encouraging results. Resection of the cystic ovary is advisable before resorting to hysterectomy in young people. Patients over 40 can be safely treated by intrauterine application of radium.

In epimenorrhea the treatment is the same. It is a speeding-up of the cycle most common after parturition and attributed to the activity of the anterior lobe persisting. In younger patients, rest, curettage and iron to combat anemia are satisfactory, with hysterectomy as a last resort. In older patients radiation following curettage is most satisfactory.

The knowledge of menstruation without ovulation has offered a new cause for sterility. Examination of the endometrium one or two days before the period is due is, therefore, essential when investigating such an individual.

Scanty menstruation with dysmenorrhea is benefited by progynon intramuscularly or orally during the first half of the interval. Menopausal symptoms respond favorably to progynon treatment orally in mild doses and by injection twice a week in severe cases. The indiscriminate use of hormones should be avoided.

F. L. ADAIR AND S. A. PEARL.

Vogt, E.: The Treatment of Undernutrition and Secondary Amenorrhea by Implantation of the Hypophysis of a Newborn and With Estrogenic and Luteal Hormones, Med. Klin. 31: 1393, 1935.

The author had under his care a thirty-three-year-old woman who exhibited severe undernutrition associated with a secondary amenorrhea. The latter had existed for sixteen years and had begun at the time of a severe attack of the grip. All known methods of therapy were tried without any beneficial effects on the patient's weight or her amenorrhea. Finally the author implanted the pituitary gland of a newborn infant into the musculature of the abdominal wall. Excellent results followed. The patient began to gain weight immediately and at the time of the report had gained 31 pounds. After the gain in weight started, the long-standing amenorrhea was treated with estrogenic and corpus luteum hormones and then menstruation took place. The patient received a total of 1,700,000 international units of estrogenic substance in six injections and 180 units of progestin in 7 injections. Bleeding took place thirty days after the beginning of the treatment.

J. P. GREENHILL.

Goldberg, M. B., and Lisser, H.: Clinical Use of Emmenin, Endocrinology 19: 649, 1935.

Emmenin-Collip, an alcohol soluble, ether insoluble complex present in acetone extracts of human placenta was given an adequate trial in 100 instances of various menstrual disorders, occurring in 66 women. It has proved helpful in restoring menstruation if periods have been absent less than a year. It is probably useless in amenorrhea of longer duration. In eight of nine cases of oligomenorrhea (delayed periods) the menstrual interval was more nearly regularized. The same result was accomplished in seven patients whose menstrual interval was utterly irregular, sometimes too soon, other times too late. Polymenorrhea (consistently too frequent periods) was unaffected by Emmenin (only 3 cases). Hypomenorrhea (scanty flow) was definitely improved in nine of twelve cases. Menopausal symptoms and cyclic menstrual headaches were relieved in a fair majority of cases. In two of four cases of sterility pregnancy occurred under Emmenin therapy. Over 60 per cent of 40 subjects with severe dysmenorrhea were remarkably relieved. Psychic factors were rigidly excluded. This constitutes its most significant clinical usefulness. Emmenin deserves a place in the therapeutics of menstrual disorders. The chief objection, at present, to its widespread use in clinical practice, is its expense.

J. THORNWELL WITHERSPOON.

Zondek, B.: Gonadotropic Stimulation Therapy, Acta obst. et gynec. Scandinav. 15: 1, 1935.

Until the present time hormone therapy has been purely substitutional. Zondek believes that in the future hormone therapy should be one of stimulation. He indicates that hormones should be administered in order to stimulate the glands which produce hormones. He emphasizes that prolactin is a gonadotropic hormone

the effect of which can be further strengthened by a synergistic factor. This synergistic factor Zondek calls "Synprolan." For the combination of prolan and synprolan the name "Prosyplan" is recommended. The anterior pituitary lobe produces and stores prolan and synprolan, whereas the urine of pregnancy contains only prolan. Zondek has definitely shown that in man as well as in animals prolan alone has a distinct gonadotropic action. It was the ability to excite into action an ovary which previously did not function, to stimulate an already functioning ovary to increased activity, and to reawaken the function of an ovary which had previously ceased to function. In a case of a twenty-two-year-old girl with primary amenorrhea and a hypoplastic uterus, Zondek was able to produce typical ovarian function by administering 15,000 rat units of prolan.

J. P. GREENHILL.

Witherspoon, J. Thornwell: The Endocrinal Origin of Primary Dysmenorrhoea and Its Hormonal Treatment, *Endocrinology* 19: 403, 1935.

The most recent explanation of primary dysmenorrhea is an endocrine imbalance. The pain of primary dysmenorrhea can be explained by the withdrawal of the progestin influence, which results in whipping into marked activity, by the action of the follicular hormone, a uterus which has been lying in a quiescent state for ten days to two weeks.

The rationale of treatment in this condition is to counterbalance the follicular hormone activity by administering the luteinizing principle found in the urine of pregnant women. The method of treatment employed was to inject intramuscularly and daily, from three to four days previous to the expected flow, and one to two days during the flow, 250 R.U. (1 c.c.) of follutein. Thirteen of seventeen patients so treated for dysmenorrhea experienced relief.

J. THORNWELL WITHERSPOON.

Hofstätter, R.: Organo Therapeutic Researches on Pineal Extract With Special Reference to Sexual Excitability, *Wien. klin. Wchnschr.* 49: 136, 1936.

The mechanism of the pineal gland is still not understood. Pineal extract has been assumed to produce a depressing effect on sexual irritability not so much by direct action on the ovary, but rather by depressing the sex centers of the mid-brain or higher cerebral centers. There may be an antagonism between the anterior lobe of the hypophysis and the epiphysis. This author over a period of twenty-two years has used an extract of pineal gland in a series of 290 cases. His subjects varied in age from five years to the climacterium and also included patients who were castrated or who had hysterectomy without castration. So far as producing a depressing effect on cases with hyperlibido, his results are variable and inconclusive. Further clinical and experimental work is necessary before definite conclusions can be given.

W. B. SERBIN.

Glass, S. J.: Migraine and Ovarian Deficiency, *Endocrinology* 20: 333, 1936.

A study was made of the prolan A and estrin relationships in 10 young migrainous women with ovarian dysfunction. Quantitative hormone essays showed a reversal of the normal ratio in the direction of increased prolan A and decreased estrin output. Estrogenic therapy tended to correct the hormonal imbalance by suppression of the prolan A secretion with concomitant relief of the migraine symptoms in 80 per cent of the cases. Prolan administration either gave no relief or

intensified the symptoms. The exact relationship of the hyperprolanism to the migraine is unknown; however, migraine associated with ovarian deficiency lends itself to a rational control with estrogenic therapy.

J. THORNWELL WITHERSPOON.

Mazer, Meranze, and Israel: Evaluation of the Constitutional Effects of Large Doses of Estrogenic Principle, J. A. M. A. 105: 257, 1935.

From a survey of the literature and the clinical study of 30 patients, it was found that injections of from 100,000 to 200,000 rat units of estrogenic substance, given in divided doses over periods of from two to three months, produce no appreciable changes in body weight, basal metabolism, blood pressure, blood count, coagulation and bleeding times, blood chemistry and urine.

In 6 of 17 regularly menstruating women, injections of these large quantities of estrogenic substance produced a temporary delay in the menstrual flow (from one to three weeks) and established in these six patients a new date of onset of the menses. This phenomenon is apparently due to a temporary inhibition of the anterior pituitary lobe.

Growth of the mammary glands and increased libido were observed in a few of the treated patients.

Relatively larger doses of the estrogenic substance (from 85,000 to 150,000 rat units) than those employed clinically produced neither macro- nor microscopic changes in the vital organs of 30 rabbits. The response of the ovaries to huge doses of the estrogenic substance is either degenerative or stimulative, depending on the species and age of the test animals and the duration of administration of the substance.

GROVER LIESE.

Joachimovits, R.: Contribution to the Treatment of Uterine Bleeding in the Prelimacterium, Wien. klin. Wchnschr. 49: 365, 1936.

In a study of 150 uteruses removed at operation from women during the preclimacteric years, the author made the following observations: There were senile changes in the uterine muscle; there was protoplasmic shrinking of the basal layers of the endometrium; hyalinization and atrophy of the uterine mucosa. On the basis of these histologic findings involving both the endometrium and the myometrium the author made injections of follicular hormone in experimental animals. He reasoned that just as the endometrium has its cycle, the myometrium likewise has its cycle. Injection of follicular hormone into experimental animals produced a myoblastosis in the uterus. If the cause of preclimacteric bleeding is muscular in origin, the injection of sex hormone to produce myoblastic islands in the uterine wall is rational. A better treatment consists in a combination of follicle hormone plus sekalin, the latter having a direct effect on the muscular wall also. In 30 cases he found this combination to give satisfactory results.

W. B. SERBIN.

Schaefer, R. L.: Menopausal Hypertension, Endocrinology 19: 705, 1935.

In the series of 13 subjects of menopausal hypertension there occurred a substantial reduction of the hypertension and amelioration of all the associated symptoms after the administration of theelin. The data secured indicate that hypertension frequently develops during the menopause and there is an evident incretory imbalance present at that time. It appears that there is an actual lack of a follicular hormone (theelin) and that its replacement is logically indicated.

J. THORNWELL WITHERSPOON.

Bishop, P. M. F.: The "Pregnancy" Test in Relation to Death of the Ovum, Lancet 2: 364, 1935.

The author reports the results of the Friedman test for death of the ovum in 11 cases. The test tends to become negative between the tenth and twenty-fourth days after intrauterine death.

When an intrauterine death is suspected a negative pregnancy reaction will confirm the suspicion but a positive reaction may be present for three months after the fetus has died. Estrin reaction becomes negative considerably sooner than the Aschheim-Zondek and Friedman tests. Yet the former may remain positive for three weeks.

The author was unable to present any additional data on factors which regulate the secretion of gonadotropic hormones by the placenta.

H. CLOSE HESSELTINE.

Campbell, K. C.: A Method for Ovarian Transplantation on Rabbits Used for the Aschheim-Zondek Test for Pregnancy, J. Lab. & Clin. Med. 20: 520, 1935.

To avoid repeated posterior or anterior laparotomies on injected rabbits a modified technic of the original Goodale and Flanagan method of ovarian transplantation is proposed. The advantages are: (1) the ovaries are readily accessible; (2) less time is required for the examination as there is only one incision to be made; (3) anesthesia is of short duration and resulting anesthetic deaths are reduced to a minimum; (4) the mortality from infection is greatly diminished; (5) the ovaries are more likely to maintain a normal appearance than is the case if the organs are handled during each examination. The procedure consists of an initial posterior laparotomy, transplantation of the ovaries into the subcutaneous areolar tissue of the back, and subsequent examination by opening the original incision and lifting the skin flaps for inspection of the ovaries. The modification permits repeated examinations after an adequate time for the ovaries to return to normal after a positive reaction. Numerous protocols are cited indicating the value of the method. Vaseline gauze has been discontinued and the incidence of infection further reduced.

W. B. SERBIN.

Witherspoon, J. Thornwell, and Collins, Conrad G.: The Etiology of Functional Puberty Bleeding and the Treatment by Hormonal Therapy, New Orleans M. & S. J. 88: 205, 1935.

Idiopathic uterine bleeding results from a hyperplastic condition of the uterine mucosa, which in turn results from ovarian dysfunction. The ovarian dysfunction results from the presence and persistence of multiple follicle cysts in the ovaries. The actual cause of the bleeding in endometrial hyperplasia is probably due to the withdrawal of estrogenic stimulation similar to that which determines the onset of the menstrual flow. The treatment of functional bleedings of puberty, after determining by bimanual examination that no pelvic pathology exists, is as follows: the daily administration of 1 c.c. of follutein, alone or in combination with 2 c.c. of the anterior pituitary growth factor, until bleeding ceases. With the onset of the next flow daily injections are again given until the flow stops. In like manner treatment is carried through a third period. No treatment is given during the fourth period in the hope that the menstrual rhythm has reestablished itself. There is a tendency to spontaneous readjustment of the functional uterine bleeding in young girls. In consequence some of the acclaimed cures might have been spontaneous cures.

EUGENE S. AUER.

Items

American Board of Obstetrics and Gynecology

The next written examination and review of case histories of Group B applicants by the American Board of Obstetrics and Gynecology will be held in various cities in the United States and Canada on Saturday, November 6, 1937.

The next general examination for all candidates (Groups A and B) will be held in San Francisco, Cal., on June 13 and 14, 1938, immediately prior to the American Medical Association meeting.

Application blanks and booklets of information may be obtained from Dr. Paul Titus, Secretary, 1015 Highland Building, Pittsburgh (6), Pennsylvania. Applications for these examinations must be filed in the Secretary's office not later than sixty days prior to the scheduled dates of examination.

American Board of Obstetrics and Gynecology

Diplomates Certified by the American Board of Obstetrics and Gynecology, Inc., June 7 and 8, 1937, Atlantic City, N. J.

The following names are to be added to the list published in the July, 1937 issue of this JOURNAL.

PAUL A. GEMPEL, Kansas City, Mo.

S. LEON ISRAEL, Philadelphia, Pa.

CONSTANTINE J. NICHOLAS, Santa Barbara, Calif.

VICTOR G. H. WALLACE, Toronto, Canada.

Advisory Board for Medical Specialties

The annual meeting of the Advisory Board for Medical Specialties, which is the coordinating Board of the twelve certifying boards in the various specialties, the Association of Medical Colleges, the American Hospital Association, the Federation of State Medical Boards of the U. S. A., and the National Board of Medical Examiners was held at Atlantic City, N. J., on June 6, 1937.

The following officers were elected:

Officers and Executive Committee

Willard C. Rappleye, M.D., *President*, New York, N. Y.

W. P. Wherry, M.D., *Vice-President*, Omaha, Neb.

Paul Titus, M.D., *Secretary-Treasurer*, Pittsburgh, Pa.

W. B. Lancaster, M.D., Boston, Mass.

R. C. Buerki, M.D., Madison, Wis.

Dr. Louis B. Wilson of Rochester, Minn., the retiring president of the Board, was elected an emeritus member of the Board.